Award Number: W81XWH-12-1-0143

TITLE: Social Resources That Preserve Functional Independence After Memory Loss

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REPORT DATE: July-2016

TYPE OF REPORT: Final Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE		*Form Approved OMB No. 0704-0188*
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1. REPORT DATE July-2016	**2. REPORT TYPE** Final	**3. DATES COVERED** 20 April 2012 – 19 April 2016
4. TITLE AND SUBTITLE: Social Resources That Preserve Functional Independence After Memory Loss		**5a. CONTRACT NUMBER** **5b. GRANT NUMBER** W81XWH-12-1-0143 **5c. PROGRAM ELEMENT NUMBER**
6. AUTHOR(S) Dr. M. Maria Glymour, Dr. Thu Nguyen, Dr. Pamela M. Rist E-Mail: mglymour@psg.ucsf.edu		**5d. PROJECT NUMBER** **5e. TASK NUMBER** **5f. WORK UNIT NUMBER**
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of California San Francisco Dept of Epidemiology and Biostatistics 550 16th Street, 2nd Floor San Francisco, CA 94143		**8. PERFORMING ORGANIZATION REPORT**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		**10. SPONSOR/MONITOR'S ACRONYM(S)** **11. SPONSOR/MONITOR'S NUMBER(S)**
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited		
13. SUPPLEMENTARY NOTES		

14. ABSTRACT *(Enter a brief (approximately 200 words) unclassified summary of the most significant finding during the research period.)*

Millions of older veterans will encounter mild to moderate memory or cognitive losses. It is critical to identify strategies to maintain functional independence and maximize quality of life for these individuals. We used a large, diverse, longitudinal study of middle aged and older Americans to identify factors that help individuals preserve functional independence as long as possible, even in the context of declining memory or memory impairment. Memory loss strongly predicted incident limitations in basic and instrumental Activities of Daily Living (I/ADLs). Physical activity predicted lower risk of incident limitations even among those with cognitive impairment, while smoking and depression may increase the risk of incident ADL limitations. Physical activity was also associated with lower risk of future nursing home admission, another powerful indicator of functional independence. Although most family level variables were not associated with independence outcomes, being married and having a spouse with more education and lower depressive symptoms predicted better functional outcomes. Finally, our results indicate that several features of neighborhood of residence, including perceived safety, disorder, and cohesion predicted IADL outcomes, in individuals with or without memory impairments. Memory impairment increases the risk of disability, but many strategies can stave off dependencies, maximize quality of life, and minimize caregiver burden. These findings lay the groundwork for policies regarding housing settings, interventions for management of chronic conditions, and interventions to provide resources for caregivers to improve functional independence in older veterans.

15. SUBJECT TERMS Disability, functional independence, activities of daily living, instrumental activities of daily living, individual, family, community, dementia, memory impairment

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION**	**18. NUMBER**	**19a. NAME OF USAMRMC RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**		**OF**	**19b. TELEPHONE NUMBER**
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Table of Contents

Page

1. INTRODUCTION

Memory losses are common among long-term survivors of traumatic brain injury (TBI) and TBI has been linked to increased risk of memory impairment and dementia. This is an important determinant of long-term well-being for military service men and women and their families, because of the elevated incidence of TBI in combat areas and the high prevalence of memory impairment in the general older population. Memory and cognitive impairments predict substantial losses in ability to independently manage daily activities; this loss of independence can be devastating to the individual and his or her family. To avoid dependence, we need to identify factors which preserve independence even in the face of memory and cognitive losses. While studies have examined predictors of institutionalization among those with dementia(*1*), factors like depression which predict institutionalization may be undertreated among those with dementia.(*2*) It is not known whether managing these risk factors among individuals with cognitive impairment is important because little research has been done on whether resources at personal and environmental levels can modify the translation of impairments caused by neurodegenerative diseases into functional disabilities. Current understanding of disability emphasizes that physical impairments in body functioning or structure do not necessarily induce functional disability because environmental, behavioral, and instrumental accommodations can foster continued independence.(*3*) Individual level modifiers for example, physical activity or not being depressed, and family level modifiers for example, spouse's education and contacts with friends and family, may also influence functional limitations and the individual's ability to use accommodations or coping strategies and may help promote functional independence even among individuals with memory loss or dementia. We proposed to use data from the nationally representative Health and Retirement Study (HRS), a large, diverse, longitudinal study of middle aged and older Americans, to identify modifiable individual-, family-, and community level factors that help individuals preserve functional independence as long as possible even in the context of declining memory or cognitive impairment.

2. KEYWORDS

Disability, functional independence, activities of daily living, instrumental activities of daily living, individual, family, community, dementia, memory impairment

3. ACCOMPLISHMENTS

What were the major goals of the project?

1. Estimate the association between memory/cognitive losses and changes in functional independence in HRS cohort members (Q3 2012)
2. Test individual level resiliency factors as modifiers of the effects of memory on functional impairments in longitudinal models (Q3 2012 through Q1 2013)
3. Link family level variables and test family level resiliency factors as modifiers of the effects of memory functional impairments (Q1 2013 through Q3 2013)
4. Test community level resiliency factors as modifiers of the effects of memory on functional impairments (Q1 2015 through Q1 2016)
5. Characterize neighborhood resources using ecometric methods, linking other data, e.g. Census and American Community Survey to (Q1 2015 to Q4 2015).
6. Summary models identifying most powerful modifiable factors promoting independence despite memory loss (Q1 2016 through Q3 2016)

What was accomplished under these goals?

- Developed inverse probability weighting models to statistically account for selective survival and dropout.
- Completed statistical programming, specified core statistical models and derived preliminary estimates of the association between cognitive loss as measured by a dementia probability score and changes in functional independence as measured by five Activities of Daily Living (ADL) and five Instrumental Activities of Daily Living (IADL) in Health and Retirement Survey (HRS) cohort members.
- Tested individual level resiliency factors as modifiers of the effects of cognitive impairment on ADL limitations using pooled logistic regression and Poisson regression as well as inverse probability weighting.
- Published a manuscript on cognitive impairment, individual-level modifiers and incident ADL limitations.
- Published a manuscript on cognitive impairment, individual-level modifiers and incident IADL limitations.
- Submitted abstracts to the American Academy of Neurology Annual Meeting in 2014 and the Society of Epidemiological Research Annual Meeting in 2014.
- Linked family level variables and tested family level resiliency factors as modifiers of the effects of memory functional impairments.
- Published manuscript presenting results from analysis of cognitive impairment, family-level modifiers, and incident I/ADL limitations.
- Published manuscript examining the influence of neighborhood level factors on incident I/ADL limitations and if these associations varied by cognitive status.
- Published manuscript estimating effects of physical inactivity, ever smoking, and not consuming alcohol on risk of nursing home admission as a measure of functional independence.

To accomplish the tasks outlined above, we first completed an analysis examining the impact of individual level modifiers on the association between cognitive impairment and incident ADL limitations. The complete manuscript of this analysis ("Dementia and dependence: Do modifiable risk factors delay disability?") was published in *Neurology* in 2014 and is available

as an appendix. In brief, we used data from individuals enrolled in the Health and Retirement Study. The sample included 4,922 Health and Retirement Study participants aged 65+ without limitations in activities of daily living (ADLs) at baseline. Participants were interviewed biennially up to 12 years. Cognitive status was assessed through a dementia probability score and a memory score, both of which were estimated from composites of direct and proxy assessments. We divided the dementia probability score and memory score into four categories representing low, mild, moderate or high probability of developing dementia or of having memory impairments. Our outcome was reported difficulty in any of the five activities of daily living (getting across a room, dressing, bathing, eating, and getting in and out of bed) in the past 30 days. We assessed whether physical activity, smoking, alcohol consumption, depression and income reduced the chances of incident ADL limitations for individuals across the categories of dementia risk and memory impairments, using pooled logistic regression models with inverse probability weights to adjust for time-varying confounding. We assessed multiplicative and additive interactions of dementia category with each modifier in predicting incident ADL limitations.

As expected, higher dementia score category was associated with an increased risk of ADL limitations (OR=1.65, 95% CI: 1.49-1.83 per category increase). On a relative scale, physical inactivity was associated with an increased risk of incident ADL limitations among those with low dementia probability (OR-1.51, 95% CI: 1.25, 1.81). Importantly, the interaction between physical activity and dementia probability was close to 1 and not significant, indicating that the estimated relative harm of low physical activity was similar regardless of dementia category.

In our next set of analyses, we calculated the marginal probability of developing any incident ADL limitations for each combination of modifier status and low or high dementia risk. These analyses addressed the impact of the modifiers on an absolute scale. We observed that smoking, not drinking and low income have larger adverse effects on the absolute probability of developing incident ADL limitations among those with high dementia probability than among those with low dementia probability. This suggested that even among individuals with substantial cognitive impairment managing conventional risk factors is very important and may provide a way to stave off dependencies, maximize quality of life and minimize caregiver burden. The next step in this research (not covered in the current proposal) would be to assess whether changes in these risk factors predict changes in ADL limitations and evaluate *who* among the population these risk factors influence the most, in order to better guide intervention development.

In addition to containing data on ADL limitations, the HRS cohort also assessed limitations in Instrumental Activities of Daily Living (IADLs). The manuscript titled “Do physical activity, smoking, drinking or depression modify transitions from cognitive impairment to functional disability?” was recently published in Journal of Alzheimer’s Disease in 2015 and is available in the appendix. The analysis sample included 5,219 HRS participants aged 65+ without activity limitations in 1998 or 2000.

Similar to the ADL analysis, we examined the impact of both memory score and dementia probability status on our outcome. We categorized memory and dementia status based on quartiles of their distributions at baseline. These categories were modeled as indicator variables due to the non-linear associations between memory impairment and incident IADL limitations. Since we were interested in examined the effect of our modifiers among those who are cognitively impaired, worst memory function or high dementia probability were used as the reference group for all analyses. Results for memory and dementia were similar so we will only discuss the results for dementia probability below.

We used the same modifiers as those used in our ADL analyses (physical activity, smoking, alcohol consumption, depression and income). Our exposure and modifier status was

assessed in the wave prior to our outcome assessment. For our outcome, we used limitations in the past 30 days in IADLs. The IADLs assessed in HRS were using a telephone, taking medication, handling money, shopping and preparing meals. Possible response options were yes, no, or do not do, which was treated as missing in this analysis. Dementia probability, categorized in quartiles, was used to predict incident IADL limitations with Poisson regression. We estimated relative (risk ratio) and absolute (number of limitations) effects from models including dementia, individual-level modifiers (physical inactivity, smoking, no alcohol consumption, and depression) and interaction terms between dementia and individual-level modifiers.

Dementia probability quartile predicted incident IADL limitations (relative risk for highest versus lowest quartile = 0.44; 95% CI: 0.28–0.70). Physical inactivity (RR = 1.60; 95% CI: 1.16, 2.19) increased the risk of IADL limitations among the cognitively impaired. The interaction between physical inactivity and low dementia probability was statistically significant (p = 0.009) indicating that physical inactivity had significantly larger effects on incident IADLs among cognitively normal than among those with high dementia probability.

In conclusion, our results suggest that maintaining physical activity should be a high priority for individuals with cognitive impairment as well as their families and clinicians because it may help to stave off dependency.

Our previous analyses have focused on the role of individual-level factors on ameliorating the impact of cognitive impairment on functional limitations. However, extensive evidence suggests that social networks also influence various domains of health, with some evidence of special importance of spouses and friends for older adults. Little is known about whether these associations prevail for onset of instrument and basic activities of daily living (I/ADLs) and whether they differ for individuals with memory impairment. The objective of the next part of our project was to determine whether family-level factors reduce the risk of incident I/ADLs and whether these associations differ for individual with high versus low dementia probability. We present an overview of our methods and results below. Our analytic sample included 4,100 Health and Retirement Study Participants Study aged ≥65 without baseline limitations in activities of daily living (ADLs) or instrumental activities of daily living (IADLs) were interviewed biennially for up to 12 years.

The family-level variables we examined in this study included living arrangements, proximity to children, contacts with friends, spouse's depression status, spouse's employment status, and spouse's education status. We estimated the risk of incident ADL or IADL limitations using pooled logistic regression controlling for individual characteristics and cognitive function. We also explored whether dementia probability status may modify the association between family-level variables and incident I/ADL limitations.

To account for selection and attrition during the course of the study, we used inverse probability weights. Those with high dementia probability at baseline were less likely be married compared to those with lower dementia probability (Table 1). 1,500 people reported any ADL limitation and 1,496 people reported any IADL limitation during the course of the study. Table 2 shows the associations between our family-level variables and the risk of incident ADL or IADL limitations. Few family-level variables predicted incident limitations. Not being married compared to being married (ADL OR=1.14; 95% CI: 1.01, 1.30), having a depressed compared to a non-depressed spouse (ADL OR=1.56, 95% CI: 1.21, 2.00) or a spouse with less than high school education (ADL OR=1.29, 95% CI: 1.06, 1.57) compared to at least high school education predicted increased risk of incident ADL but not IADL limitations. Living with someone other than a spouse compared to living with a spouse increased risk of ADL (OR-1.35; 95% CI: 1.11, 1.65) and IADL (OR=1.30; 95% CI: 1.06, 1.61) limitations. Effects did not vary by dementia probability (Table 3). The paper presenting these results were published in the American Journal of Geriatric Psychiatry in 2016 and is available in the appendix.

We undertook analyses to determine whether low neighborhood disorder, high neighborhood safety, social cohesion, and social ties reduced the incidence of I/ADL limitations and whether these relationships were modified by memory function. The neighborhood can represent an older adult's primary environmental context. As health declines (*4*) or the elder becomes unable to drive (*5*), more time is spent in the local community. Neighborhood social ties, perception of neighborhood safety, and neighborhood physical disorder can facilitate or restrict movement and independence.

Beginning in 2006, questions assessing neighborhood physical disorder and social cohesion were posited in each biennial HRS wave to a rotating, random sample of 50% of the core participants who completed the enhanced face to face interview. This study utilizes 2006 and 2008 data. Neighborhood variables assessing safety and social ties were asked of all the core participants in every biennial wave, but to have consistency with the timing of the neighborhood measures above, for participants answering questions regarding physical disorder and social cohesion in 2006, we used data on safety and social ties from 2006. Likewise, for participants with data on physical disorder and social cohesion in 2008, we used data for the other neighborhood variables from 2008. We fitted pooled logistic models and controlled for individual characteristics, demographics, health behaviors, and comorbidities.

In this study, we investigated four community-level factors: physical neighborhood disorder, social cohesion, neighborhood safety, and neighborhood social interaction. Participants were asked to assess the neighborhood physical order by the presence of vandalism/graffiti, vacant or deserted houses, cleanliness of the area, and whether respondents would be afraid walking home at night. The social cohesion scale measured feelings of trust, feeling part of the area, whether the respondent thinks people are friendly or would help them if they were in trouble. HRS respondents were asked how they would rate the safety of their neighborhood with response items being excellent, very good, good, fair, or poor. Lastly, we assessed social ties to neighbors. Participants were asked if they had friends in the neighborhood and separately if they had relatives in the neighborhood. They were also asked how often they get together with neighbors for a social visit. We created a composite measure defined as the mean of the four individual neighborhood measures.

After adjustment for demographics and socioeconomic status (model 2), neighborhood characteristics were associated with IADL incidence: (physical disorder OR=0.51 comparing the lowest to highest possible neighborhood physical disorder (95% CI: 0.37,0.69)); neighborhood social cohesion (OR=0.46 comparing highest to lowest cohesion (95% CI: 0.34, 0.62)); neighborhood safety (OR=0.59 comparing ratings of excellent/very good/ good vs fair/poor (95% CI: 0.46, 0.76)); and the composite neighborhood measure (OR=0.31 (95% CI: 0.20, 0.48)). These neighborhood characteristics were also associated with incidence of ADL limitations (physical disorder OR=0.59 (95% CI: 0.43, 0.81)); social cohesion OR=0.60 (95% CI: 0.45, 0.81); safety OR=0.74 (95% CI: 0.58, 0.93); composite OR=0.49 (95% CI: 0.32, 0.76). Neighborhood social ties were not related to IADLs (OR=0.93 (95% CI: 0.74, 1.17)) or ADLs (OR=1.01 (95% CI: 0.80, 1.28) (Table 5).

Low neighborhood physical disorder, high social cohesion, and high safety were protective for onset of IADLs among participants with normal memory but the effects were attenuated and not statistically significant among participants with memory impairment (Table 6). P-values for interaction between memory and each of the neighborhood characteristics were as follows: social cohesion: <0.001, physical disorder p-value:<0.01; neighborhood safety p-value:0.05; social ties p-value:0.02; composite p-value:<0.001). In contrast, there was no evidence of interactions on the relative scale between any of the neighborhood factors and memory function ($p \geq 0.1$ for all interactions) for onset of ADLs (table 6. Stratified results by memory function and neighborhood characteristics are presented in Table 7.

The next priority areas for this research area are to understand whether effects are similar for veterans or other populations. The final task for this year's annual report was to "Link each study participants to census tract (CT) of residence at each interview wave." We experienced substantial delays in accessing the HRS census tract data, because the HRS approval process changed. We have now completed the process of meeting the data storage requirements to work with this restricted data in the HRS at UCSF. We have been granted access to the data. The final paper is preparation, and we anticipate it will be submitted in the next 6 months. The funding for this remaining work will be supported by Maria Glymour's discretionary fund at UCSF.

The original scope of the grant, which intended to identify social resources that preserve functional independence after memory loss, focused on conventional I/ADL measures as measures of 'functional independence." We realized that in our data nursing home admission is another extremely valuable measure of functional independence, so we applied the methods developed for this grant to examine nursing home admission as an outcome event. These analyses should be especially informative for risk factors that were found to affect either instrumental or basic ADL limitations, but not both: in some ways nursing home admission provides an even more powerful indicator of dependence. Cognitive impairment strongly predicts risk of nursing home admission(*6, 7*), more than doubling the risk of nursing home admission according to a large meta-analysis.(*6*) Given the strong association between cognitive function and risk of nursing home admission, there is a growing interest in finding factors which may delay nursing home placement even among those with cognitive impairment. Using methods which we developed as part of this grant, we have performed analyses examining effect of cognitive status and modifiable risk factors on the risk of nursing home admission. We also evaluated interactions between cognitive status and each risk factor to determine if the relative or absolute impact of each modifiable factor differs based on the individual's cognitive status. We hypothesized that physical inactivity, not consuming alcohol, and ever smoking would predict nursing home admission among individuals with normal cognitive function, but effects of these risk factors would be attenuated in both relative and absolute terms among individuals with impaired cognition.

The risk factors considered in our first analyses were physical inactivity, not consuming alcohol, and ever smoking. In addition to including dichotomized dementia probability, physical activity, alcohol consumption, and smoking status, all analyses were adjusted for demographics, socioeconomic status, and comorbidities. Our sample for these analyses included 7,631 HRS participants in the 2000 interviews who were age 65 or older and did not report a nursing home stay or living in a nursing home in 1998 or 2000. During follow-up, 2,353 people reported admission to a nursing home.

Table 8 shows the association between our risk factors and low dementia probability and risk of nursing home admission. Those with low dementia probability had roughly half the risk of nursing home admission during each two-year interview interval (RR = 0.49; 95% CI: 0.41, 0.59) compared to those with high dementia probability. Physical inactivity compared to being active (RR = 1.27; 95% CI: 1.15, 1.41), ever smoking compared to never smoking (RR = 1.12; 95% CI: 1.01, 1.25), and not consuming alcohol (RR = 1.28; 95% CI: 1.13, 1.45) or heavy alcohol consumption (RR = 1.44; 95% CI: 1.13, 1.82) compared to moderate alcohol consumption predicted increased risk of nursing home admission.

We next examined whether these factors had different effects among individuals at risk of dementia than among cognitively normal elders. There was no statistically significant interaction between dementia probability and physical inactivity ($p = 0.92$), smoking ($p = 0.40$), no alcohol consumption ($p = 0.28$) or heavy alcohol consumption ($p = 0.69$), indicating that the relative harm of the modifier was similar for those with low and high dementia probability (Table 9).

Because similar relative effects may conceal differences in absolute effects, we also estimated the marginal probability of nursing home admission for each risk factor among those with high and low dementia probability (Fig. 1). Physical activity was associated with an decreased absolute probability of nursing home admission for those with low dementia probability. However, the magnitude of the estimated effect of physical activity on the probability of nursing home admission was slightly higher among those with high dementia probability (2.39% point difference) than among those with low dementia probability (1.55% point difference). Never smoking was not associated with significantly lower probability of nursing home admission among those with high dementia probability; the estimated absolute effect among the high dementia probability group (2.55% point difference) was larger than among the low dementia probability (0.07% point difference) group but this difference was not statistically significant. Moderate drinking compared to not consuming alcohol predicted lower risk of nursing home admission among those with low dementia probability (1.40% point difference) and among those with high dementia probability (4.84% point difference). Moderate drinking compared to heavy drinking predicted lower risk of nursing home admission among those with low dementia probability (2.48% point difference) but not among those with high dementia probability (1.33% point difference). These results have been recently published in Archives of Gerontology and Geriatrics and is available in the appendix.

CONCLUSION

We found strong associations between decreased cognitive functioning and incident ADL limitations. Smoking, not drinking, and having low income may increase the risk of incident ADL limitations among those with cognitive impairments. Physical inactivity was associated with an increased risk of incidence IADL limitations, even among the cognitively impaired. We recently expanded the operationalization of independence in this research project to examine the influence of these individual level factors on nursing home admission risk. We observed that physical activity, moderate alcohol consumption, never smoking lowered the risk of nursing home admission and the relative effects of these factors were similar for those with low and high dementia probability. In addition to our work examining the impact of individual-level factors on incident I/ADL limitations, we have also explored whether family-level modifiers influence the onset of I/ADL limitations. We observed that older adults who are not married, live with someone other than their spouse, or whose spouses have elevated depressive symptoms or low education are at higher risk of ADL limitation onset. Our investigation of neighborhood-level modifiers indicated that social cohesion, low physical disorder, and neighborhood safety reduced the risk of incident IADL limitations. These associations did not vary by cognitive function. These findings have critical importance for clinicians, patients, and family members of individuals with cognitive impairments or incipient dementia. By managing conventional risk factors and residing in a cohesive, safe, and well-maintained neighborhood, it may be possible to stave off dependencies and reduce nursing home admission risk. Additionally, spousal resources may be important opportunities to prevent disability.

Disseminating these results is particularly important because conventional risk factors for ADL limitations like depression are often undertreated among those with cognitive impairment.(*2*) Even traditional vascular risk factors like high blood pressure, dyslipidemia, diabetes mellitus, smoking and atherosclerotic disease may be untreated in those with cognitive impairment. Maintaining healthy risk factor profiles may help individuals with incipient dementia to maintain functional independence, and thereby lower their risk for institutionalization and decrease care-giver burden. The next stages of research are needed to guide intervention and translational work, including evidence that associations we observe are causal (and therefore

late life changes may still be beneficial) and identify individuals most likely to benefit from these interventions. The findings have the potential to substantially improve the quality of life of adults with memory impairments, reduce caregiving demands for family members, and delay institutionalization. This is especially important for older veterans and those with prior exposure to mild, moderate, or severe TBI, who are at elevated risk of memory loss and dementia. As the number of warfighters surviving TBI or other causes of cognitive impairment grows, it is crucial to identify the resources and tools that provide the greatest benefit to those individuals. Findings from this research can help provide guidance to individuals and families as well as clinicians, military planners, and policy makers.

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

Our primary dissemination method to date has been via the scientific literature, because at this early stage of research, other researchers considering intervention design are the primary audience.

What do you plan to do during the next reporting period to accomplish the goals?

Nothing to Report.

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7. M. Luppa *et al.*, Prediction of institutionalization in the elderly. A systematic review. *Age and ageing* **39**, 31 (Jan, 2010).

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

We have expanded the knowledge of modifiable factors to preserve functional independence. Previously, little has been done to understand whether these factors are important among the cognitively impaired. We have comprehensively examined individual, family, as well as community-level factors that can be leveraged to optimize quality of life, prevent or delay dependencies, and minimize caregiver burden.

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

This project has identified several points of intervention that can be used to improve the health and well-being of those at risk for functional limitations and nursing home admissions. These findings are relevant for health care providers, patients, and family members of individuals with cognitive impairments or incipient dementia. Not smoking, being physically active, having spousal support, and residing in a safe, clean, cohesive neighborhood appear protective in preserving functional independence.

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

Nothing to Report

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

6. PRODUCTS

Publications:

Rist PM, Liu SY, Glymour MM. Families and disability onset: are spousal resources less important for individuals at high risk of dementia? *Am J Geriatr Psychiatry*. 2016 Jul;24(7):585-94. doi: 10.1016/j.jagp.2016.02.003. Epub 2016 Apr 5.

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Rist P, Capistrant B, Wu Q, et al. 2014. Dementia and dependence: Do modifiable risk factors delay disability? Neurology 82(17):1543-1550.

Presentations:

Rist P, Marden J, Capistrant B, et al. 2014. Forgetful but not disabled: Predictors of incident IADL limitations. American Academy of Neurology Annual Meeting.

Rist P, Marden J, Capistrant B, et al. 2013. From forgetful to disabled: Does physical inactivity accelerate onset of IADL limitations for memory impaired adults? Society of Epidemiology Annual Conference, Seattle, WA.

Rist P, Wu Q, and Glymour M. 2012. Do social and behavioral factors protect cognitively impaired adults from functional impairments? Gerontological Society of America Annual Meeting.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

NAME	**Maria Glymour, ScD, MS**
Project Role	Principal Investigator
Researcher Identifier	None
Nearest Person Month Worked	~5.4
Contribution to Project	Principal Investigator
Funding Support	No other funding source provided funds for this project
Change in Active Support	Effective 3/1/15, Dr. Glymour began receiving 25% funding support on a Robert Wood Johnson Foundation award, "Launching the Culture of Health Investigator-Initiated Research program" Dr. Nancy E. Adler and David Vlahov, Project Directors. Dr. Glymour serves as an Associate Director and will provide a summary of the Culture of Health in Communities and participate, along with the directors, in the development of the PA and dissemination efforts.
Other Organizations Involved	Nothing to Report

NAME	**Thu Thi Nguyen, PhD**
Project Role	Specialist
Researcher Identifier	None
Nearest Person Month Worked	~9.5
Contribution to Project	Dr. Nguyen has been lead analyst on this project, developing code to characterize neighborhood variables, integrating the 2006 and 2008 samples and validating the measures. She has implemented the models for neighborhood variables predicting onset of I/ADL limitations and has written the manuscript for that work. She has also served as technical reviewer for the statistical code for the family level paper.
Funding Support	No other funding source provided funds for this project
Change in Active Support	Nothing to Report
Other Organizations Involved	Nothing to Report

NAME	**Pamela Rist**
Project Role	Postdoctoral fellow
Researcher Identifier	~5.5
Nearest Person Month Worked	6 for first year at HSPH

Contribution to Project	Pamela Rist has been an analyst on the project. She has written the manuscripts looking at individual and family level predictors of functional independence. She has also led the analyses and written the manuscript examining modifiable factors for nursing home admission. She served as technical reviewer for the neighborhood level paper.
Funding Support	No other funding source provided funds for this project
Change in Active Support	Nothing to Report
Other Organizations Involved	Nothing to Report

NAME	**Florencia Rojo**
Project Role	Graduate Student
Researcher Identifier	None
Nearest Person Month Worked	~0.18
Contribution to Project	Florencia Rojo has served as research assistant on the project, reviewing documentation on the variables, managing paperwork for the restricted data applications, and completing literature reviews, in addition to myriad smaller project related tasks.
Funding Support	No other funding source provided funds for this project
Change in Active Support	Nothing to Report
Other Organizations Involved	Nothing to Report

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

ACTIVE

(THIS AWARD)
UCSF/Glymour 04/20/13-04/19/16 1.80
Calendar
US ARMY W81XWH-12-1-0143
Social Resources that preserve functional independence after memory loss
Dr. Glymour uses a large, diverse, longitudinal study of middle aged and older Americans to identify modifiable social factors that help individuals preserve functional independence as long as possible, even in the context of declining memory or cognitive impairment.
Role: PI

UA-Birmingham/V. Howard 09/30/13 -05/31/16 1.20
Calendar

NIH/NIA 5RO1AG039588
Childhood SES Factors: Impact on age-related cognitive and vascular health
Dr. Glymour's primary roles are overseeing the data collection efforts for historical school quality measures,
working with the investigative team on collecting other measures of childhood adversity, and collaborating on
analyses and publications related to the project.
Role: PI of subcontract

Univ MN/T. Osypuk 09/12/13-09/11/16 1.20 Calendar
NIH/NIMHD 7RO1MD006064
Effect of a neighborhood experiment on youth behavior problems
Dr. Glymour assists with analytic issues related to variable creation, model building, and model interpretation related to the instrumental variable analysis of the experimental data.
Role: PI of subcontract

UCSF/N. Adler 03/01/15-02/28/18 3.00 Calendar
Robert Wood Johnson Foundation
Supporting a culture of health: The COHIR NPO
This grant establishes the National Program Office for the broad, innovative "culture of health investigator-initiated research" (COHIR) program of the RWJF at the Center for Health and Community at UCSF. We will put out a Call for Proposal and review grant applications and award grants to build the evidence to support a Culture of Health.
Role: Participating PI

Brown/Jones 07/01/15-06/30/20 1.20 Calendar
NIH/ RFA-AG-15-015
Psychometric Integrative Technology for Cognitive Health Research
The goal of the project is to harmonize brief cognitive assessments across diverse international samples and advise on the optimal measures for harmonized cross-national cohorts sponsored.
Role: Co-Investigator

Univ WA/ Crane 07/01/15-6/30/17 0.72 calendar
NIH/NIA 1A01AG042437
Genetic architecture of memory and executive functioning in Alzheimer's disease
Dr. Glymour's primary role is to serve as an advisor on Mendelian Randomization studies.
Role: PI of subcontract

Univ WA/ Crane 09/01/16-8/31/19 0.60 Calendar
DOD

Kaiser/Whitmer 12/01/15-11/30/20 1.20 calendar
Neuroepidemiology, causal inference in longitudinal observational data, health disparities, lifecourse epidemiology

Dr. Glymour will work closely with the PIs, Drs. Whitmer, Mungas, and Reed, in specification of the lifecourse models for cognitive decline, evaluating how time-varying exposures influence long-term trajectories.
Role: multiple PI

Univ MN/T. Osypuk 09/15/15-08/31/17 1.20 Calendar
NIH P0506737
Mediators and Moderators of a Neighborhood Experiment on Alcohol Use
Dr. Glymour will assist with implementing IV models using this RCT to evaluate neighborhood determinants of adolescent alcohol use.
Role: PI of subcontract

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS: None

9. APPENDICES:

All figures and/or tables referenced in the body of the report under 3.

Table 1. Characteristics of Those Included in the Analysis of Dementia Probability Category and Any Incident ADL Limitation by Dementia Probability Category at first exposure wave.

Characteristic	High Dementia Probability (N=1032)	Low Dementia Probability (N=3093)
Age (mean, std)	76.1 (6.3)	71.5 (5.2)
Gender (% male)	56.4	39.1
Race (% black)	14.5	7.5
Southern birthplace (%)	15.8	12.3
Years of education (mean, std)	11.3 (3.2)	13.0 (2.6)
Mother had ≥8 years of education (%)	44.5	55.0
Father had ≥8 years of education (%)	39.9	47.1
Physically inactive (%)	54.8	48.5
Not drinking moderately (%)	78.8	71.2
Ever smoker (%)	59.2	56.1
Current depression (%)	10.3	7.4
Body mass index (mean, std)	25.8 (4.0)	26.2 (4.3)
Number of comorbidities (mean, std)	1.6 (1.2)	1.5 (1.1)
Living arrangement		
Live with spouse	55.0	62.7
Live with others/children	11.1	8.4
Live alone	33.9	28.9
Proximity to children		
Live with children	16.6	14.7
No children	7.6	7.5
Children within 10 miles	46.6	44.2
Children over 10 miles	29.3	33.6
Less than weekly contact with friends	37.7	39.1
Spouse's employment status		
Retired	34.80	39.5
Full time	2.1	4.2
Part time	6.5	10.3
Not working/disabled	11.6	8.7
No spouse	45.0	37.3
Spouse's depression status		
Not depressed	48.3	58.2
Depressed	6.8	4.5
No spouse	45.0	37.3
Spouse's educational status		
High school diploma/GED	36.1	37.2
College diploma or higher	6.8	14.9
Less than a high school diploma/GED	12.3	10.6
No spouse	44.9	37.3
Isolation Index		
Not isolated	38.4	39.8
Isolated (1 point)	45.5	46.2

Isolated (2 points)	15.5	12.8
Isolated (3 points)	0.9	1.2
Marital Status		
Not married	44.9	37.3
Married	55.1	62.7

Table 2. Association between family-level variables and risk of incident I/ADL limitations.

	ADL			IADL		
	OR	95%	CI	OR	95%	CI
Marital Status						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.63
Married	1.00	ref		1.00	ref	
Not married	1.14	1.01	1.30	1.04	0.92	1.18
Living Arrangement						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.63
Live with spouse	1.00	ref		1.00	ref	
Live with someone other than spouse	1.35	1.11	1.65	1.30	1.06	1.61
Live Alone	1.10	0.96	1.25	0.99	0.87	1.13
Proximity to Children						
Low dementia probability	0.76	0.66	0.88	0.56	0.49	0.64
Live with children	1.00	ref		1.00	ref	
No children	0.95	0.75	1.22	0.79	0.62	1.01
Children within 10 miles	0.89	0.75	1.05	0.93	0.79	1.11
Children over 10 miles	0.87	0.73	1.04	0.87	0.73	1.04
Contacts with friends						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.64
Weekly or more frequent contact	1.00	ref		1.00	Ref	
Less than weekly contact	1.03	0.92	1.15	1.06	0.95	1.19
Spouse's employment status						
Low dementia probability	0.76	0.66	0.87	0.56	0.48	0.64
Retired spouse	1.00	ref		1.00	ref	
Spouse employed full time	0.92	0.64	1.33	0.79	0.54	1.17
Spouse employed part time	0.98	0.79	1.22	0.93	0.75	1.17
Spouse not working	1.06	0.86	1.32	0.92	0.73	1.15
No spouse	1.14	1.001	1.31	1.01	0.89	1.16
Spouse's depression status						
Low dementia probability	0.77	0.67	0.88	0.56	0.48	0.64
Not depressed spouse	1.00	ref		1.00	ref	
Depressed spouse	1.56	1.21	2.00	1.23	0.93	1.63
No spouse	1.19	1.05	1.35	1.06	0.93	1.20
Spouse's educational status						
Low dementia probability	0.76	0.66	0.87	0.56	0.48	0.64
Spouse with less than high school education	1.29	1.06	1.57	0.83	0.68	1.01
Spouse with high school education	1.00	ref		1.00	Ref	
Spouse with college education	1.03	0.84	1.26	0.98	0.80	1.21
No spouse	1.23	1.06	1.43	0.99	0.86	1.14
Isolation Index						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.64
Not isolated	1.00	ref		1.00	ref	
Isolated (1 point)	1.06	0.94	1.20	0.97	0.86	1.10
Isolated (2 points)	1.07	0.90	1.27	1.00	0.84	1.18
Isolated (3 points)	0.97	0.63	1.47	0.74	0.42	1.30

Table 3. Association between dementia probability and incident I/ADL limitations including interactions between dementia probability and family-level factors.

	ADL			IADL		
	OR	95%	CI	OR	95%	CI
Marital Status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.77	0.64	0.92	0.55	0.46	0.66
Not married	1.00	ref		1.00	ref	
Married	1.16	0.92	1.45	1.04	0.83	1.29
Married*low dementia probability	0.98	0.76	1.26	1.01	0.79	1.29
Living Arrangement						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.77	0.64	0.92	0.55	0.46	0.66
Live with spouse	1.00	ref		1.00	ref	
Live with someone other than spouse	1.22	0.83	1.78	1.24	0.86	1.77
Low dementia probability*Live with someone other than spouse	1.17	0.76	1.79	1.08	0.71	1.64
Live Alone	1.16	0.91	1.47	1.00	0.80	1.27
Low dementia probability*Live Alone	0.92	0.71	1.21	0.98	0.75	1.28
Proximity to Children						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.71	0.51	0.98	0.61	0.45	0.84
Live with children	1.00	ref		1.00	ref	
No children	0.70	0.45	1.11	0.72	0.47	1.10
Low dementia probability*No children	1.55	0.91	2.64	1.15	0.69	1.93
Children within 10 miles	0.89	0.65	1.21	1.00	0.74	1.33
Low dementia probability*Children within 10 miles	1.00	0.70	1.43	0.91	0.64	1.29
Children over 10 miles	0.80	0.57	1.12	1.00	0.73	1.38
Low dementia probability*Children over 10 miles	1.13	0.77	1.67	0.81	0.55	1.19
Contacts with friends						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.77	0.65	0.91	0.55	0.47	0.66
Weekly or more frequent contact	1.00	ref		1.00	ref	
Less than weekly contact	1.04	0.84	1.29	1.06	0.86	1.31
Low dementia probability*Less than weekly contact	0.98	0.76	1.26	1.00	0.78	1.28
Spouse's employment status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.83	0.67	1.04	0.54	0.44	0.67
Retired spouse	1.00	ref		1.00	ref	
Spouse employed full time	0.46	0.14	1.53	1.24	0.58	2.69
Low dementia probability*Spouse employed full time	2.15	0.61	7.55	0.57	0.23	1.38

Spouse employed part time	1.34	0.87	2.04	0.74	0.46	1.19
Low dementia probability*Spouse employed part time	0.67	0.41	1.10	1.35	0.79	2.30
Spouse not working	1.29	0.91	1.83	0.90	0.63	1.30
Low dementia probability*Spouse not working	0.74	0.48	1.15	1.02	0.65	1.59
No spouse	1.23	0.96	1.59	0.99	0.78	1.25
Low dementia probability*No spouse	0.90	0.68	1.20	1.04	0.79	1.36
Spouse's depression status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.76	0.63	0.92	0.54	0.45	0.65
Not depressed spouse	1.00	ref		1.00	ref	
Depressed spouse	1.42	0.92	2.18	1.11	0.69	1.79
Low dementia probability*Depressed spouse	1.16	0.68	1.97	1.18	0.66	2.11
No spouse	1.20	0.95	1.52	1.04	0.83	1.30
Low dementia probability*No spouse	0.99	0.76	1.28	1.03	0.80	1.32
Spouse's educational status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.82	0.66	1.03	0.59	0.48	0.73
Spouse with less than high school education	1.49	1.05	2.11	0.93	0.66	1.31
Low dementia probability*Spouse with less than high school education	0.82	0.54	1.23	0.84	0.55	1.27
Spouse with high school education	1.00	ref		1.00	ref	
Spouse with college education	1.18	0.75	1.84	1.15	0.73	1.82
Low dementia probability*Spouse with college education	0.84	0.52	1.38	0.81	0.49	1.33
No spouse	1.32	1.02	1.71	1.02	0.80	1.31
Low dementia probability*No spouse	0.90	0.68	1.20	0.95	0.72	1.25
Isolation Index						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.78	0.63	0.98	0.54	0.44	0.67
Isolation (1 pt)	1.13	0.90	1.43	0.96	0.76	1.20
Isolation (1 pt)*Low dementia probability	0.91	0.69	1.19	1.02	0.79	1.34
Isolation (2 pts)	1.01	0.73	1.40	0.93	0.69	1.27
Isolation (2 pts)*Low dementia probability	1.09	0.75	1.58	1.11	0.77	1.59
Isolation (3 pts)	1.02	0.56	1.85	0.83	0.28	2.44
Isolation (3 pts)*Low dementia probability	0.93	0.41	2.07	0.85	0.24	3.05

Table 4. Baseline characteristics of participants included in the analysis examining neighborhood-level factors and I/ADL limitations

Characteristic	ADL analyses (n=8801)	IADL analyses (n=9156)
Age (mean, std)	65.7 (9.8)	65.7 (9.7)
Male (%)	40.7	40.5
Black (%)	11.5	11.8
Southern birthplace (%)	14.6	14.9
Years of education (mean, std)	13.2 (2.6)	13.2 (2.5)
Mother had ≥8 years of education (%)	62.7	62.3
Father had ≥8 years of education (%)	53.0	52.6
Marital Status, (%)		
Married	72.5	72.0
Divorced/separated	9.6	9.9
Widowed	15.2	15.5
Never married	2.7	2.6
Currently employed (%)	45.1	44.8
Log household-size adjusted wealth (mean, std)	11.6 (2.7)	11.6 (2.7)
Log household-size adjusted income (mean, std)	10.4 (1.1)	10.4 (1.1)
Self-rated health (excellent, very good, good vs fair, poor) (%)	85.9	84.9
Depressive symptoms (≥3) (%)	9.0	9.4
Physically inactive (≤ 1 vigorous physical activity per week) (%)	71.2	71.8
Overweight (BMI = 25-29 kg/m2) (%)	40.5	40.1
Obese (BMI ≥ 30 kg/m2) (%)	25.9	27.5
Moderate alcohol consumption (more than 0 and fewer than 2 drinks/day) (%)	32.5	32.4
Heavy drinking alcohol consumption (2+ drinks/day) (%)	6.5	6.6
Ever smoked (%)	56.0	56.0
Memory score ≥ 0.78 (20th percentile) (%)	80.2	80.4
Neighborhood physical disorder (mean, std)	0.2 (0.2)	0.2 (0.2)
Neighborhood cohesion (mean, std)	0.8 (0.2)	0.8 (0.2)
Neighborhood safety (% excellent, very good, good)	93.3	93.5
Neighborhood social ties (mean, std)	0.6 (0.3)	0.6 (0.3)

Table 5. Associations between neighborhood level variables, IADL, and ADL limitations

	Model 1			Model 2			Model 3		
	OR	95% CI		OR	95% CI		OR	95% CI	
Onset of IADLs (n=8,726)									
Neighborhood physical disorder	0.36	0.26	0.48	0.51	0.37	0.69	0.57	0.41	0.78
Neighborhood social cohesion	0.36	0.27	0.47	0.46	0.34	0.62	0.54	0.40	0.73
Neighborhood safety	0.50	0.39	0.64	0.59	0.46	0.76	0.67	0.51	0.87
Neighborhood social ties	0.97	0.77	1.21	0.93	0.74	1.17	0.95	0.76	1.20
Composite measure	0.21	0.14	0.33	0.31	0.20	0.48	0.40	0.26	0.63
Onset of ADLs (n=8,345)									
Neighborhood physical disorder	0.43	0.32	0.58	0.59	0.43	0.81	0.70	0.50	0.96
Neighborhood social cohesion	0.46	0.34	0.61	0.60	0.45	0.81	0.79	0.58	1.08
Neighborhood safety	0.61	0.48	0.78	0.74	0.58	0.93	0.87	0.68	1.10
Neighborhood social ties	0.98	0.77	1.23	1.01	0.80	1.28	1.04	0.82	1.32
Composite measure	0.32	0.21	0.49	0.49	0.32	0.76	0.71	0.45	1.10

All neighborhood measures have a range of 0–1, so the ORs are directly comparable across the variables, and coefficients for physical disorder, social ties, social cohesion, and the composite measure represent the contrast between best possible and worst possible value (1 vs 0). For safety, the comparison is between those who rated their neighborhood as excellent, very good, or good versus those who rated their neighborhood as fair or poor.

The coefficient for normal memory represents the comparison of participants with normal memory (≥20th centile) to participants with impaired memory (<20th centile) on incidence of IADL limitations; because of the interaction term included in the model, this estimate applies to participants with the worst possible neighbourhood characteristic score (0).

Model 1 covariates: age, sex, race, memory, wave

Model 2 covariates: Model 1 + southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), marital status (married, divorced/separated, widowed, never married), mother's and father's education (=<8 years, >8 years), height, height*sex interaction, log of household size-adjusted wealth, log of household size-adjusted income, and employment status (currently working for pay, not working for pay).

Model 3 covariates: Model 2 + self-reported health (poor, fair versus good, very good, excellent), body mass index (<25, 25-29, 30+), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), physical activity (active versus inactive), alcohol consumption (no drinks, more than zero and fewer than 2 drinks /day, 2+ drinks/day), ever smoked (yes/no), depression (yes/no where yes was defined as reporting ≥3 depressive symptoms on a modified 8-item Centers for Epidemiologic Studies-Depression (CES-D) scale in the past two weeks).

Table 6. Association between neighborhood-level variables and incident IADL limitations including interactions between neighborhood variables and memory function (n=8,726)

	Model 1				Model 2				Model 3			
	OR	95% CI		p value	OR	95% CI		p value	OR	95% CI		p value
Neighborhood physical disorder												
Normal memory	1.30	0.84	2.03	0.24	1.18	0.74	1.87	0.49	1.10	0.68	1.75	0.70
Neighborhood physical disorder	1.37	0.91	2.05	0.14	0.90	0.59	1.38	0.63	0.91	0.59	1.41	0.67
Normal memory*Disorder†	2.95	1.71	5.11	<0.001	0.41	0.23	0.73	<0.01	0.49	0.27	0.87	0.01
Neighborhood social cohesion												
Normal memory	1.37	0.88	2.13	0.16	1.33	0.85	2.09	0.21	1.23	0.77	1.96	0.39
Neighborhood social cohesion	0.74	0.50	1.10	0.13	0.88	0.59	1.33	0.56	0.94	0.61	1.44	0.77
Normal memory*Cohesion†	0.32	0.19	0.54	<0.0001	0.36	0.21	0.62	<0.001	0.42	0.24	0.74	<0.01
Neighborhood safety												
Normal memory	1.09	0.70	1.69	0.71	0.93	0.59	1.47	0.76	0.92	0.57	1.46	0.72
Neighborhood safety	0.81	0.57	1.15	0.23	0.82	0.57	1.18	0.28	0.88	0.61	1.27	0.51
Normal memory*Safety†	0.49	0.32	0.77	<0.01	0.63	0.40	1.00	0.05	0.67	0.42	1.08	0.10
Neighborhood social ties												
Normal memory	0.81	0.59	1.12	0.20	0.83	0.60	1.15	0.27	0.86	0.62	1.19	0.36
Neighborhood social ties	1.45	1.04	2.04	0.03	1.34	0.95	1.89	0.09	1.35	0.95	1.92	0.10

Normal memory*Social Ties†	0.56	0.36	0.86	0.01	0.59	0.38	0.92	0.02	0.61	0.39	0.96	0.03
					Composite variable							
Normal memory	2.51	1.34	4.70	0.00	2.07	1.09	3.93	0.03	1.82	0.95	3.51	0.07
Composite measure	0.83	0.44	1.56	0.56	0.96	0.50	1.86	0.91	1.07	0.54	2.10	0.85
Normal memory*Composite†	0.14	0.06	0.32	<0.0001	0.20	0.09	0.45	<0.001	0.25	0.11	0.57	<0.01

All neighborhood measures have a range of 0–1, so the ORs are directly comparable across the variables, and coefficients for physical disorder, social ties, social cohesion, and the composite measure represent the contrast between best possible and worst possible value (1 vs 0). For safety, the comparison is between those who rated their neighborhood as excellent, very good, or good versus those who rated their neighborhood as fair or poor.

The coefficient for normal memory represents the comparison of participants with normal memory (≥20th centile) to participants with impaired memory (<20th centile) on incidence of IADL limitations; because of the interaction term included in the model, this estimate applies to participants with the worst possible neighbourhood characteristic score (0).

†The interaction coefficient for memory by neighborhood characteristic represents the estimated differential effect of the neighborhood characteristic on incidence of IADL limitations among those with normal memory ($\geq 20^{th}$ percentile) compared to those with impaired memory ($<20^{th}$ percentile). An interaction coefficient <1 indicates the effect of the neighborhood characteristic is more strongly and inversely associated with IADL limitations among those with normal memory than those with impaired memory.

Model 1 covariates: age, sex, race, memory, wave

Model 2 covariates: Model 1 + southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), marital status (married, divorced/separated, widowed, never married), mother's and father's education (=<8 years, >8 years), height, height*sex interaction, log of household size-adjusted wealth, log of household size-adjusted income, and employment status (currently working for pay, not working for pay).

Table 7. Association between neighborhood level variables and I/ADL limitations by memory status

	Model 2: Low memory			Model 2: Normal Memory		
ADLs	OR	95% CI		OR	95% CI	
Physical disorder	0.59	0.38	0.93	0.57	0.37	0.86
Social cohesion	0.49	0.32	0.73	0.68	0.45	1.01
Safety	0.81	0.57	1.14	0.70	0.52	0.96
Social ties	1.33	0.94	1.88	0.91	0.68	1.23
Composite measure	0.56	0.30	1.06	0.46	0.26	0.81
IADLs						
Physical disorder	0.77	0.50	1.18	0.39	0.26	0.59
Social cohesion	0.78	0.52	1.19	0.33	0.23	0.49
Safety	0.73	0.51	1.07	0.54	0.39	0.73
Social ties	1.37	0.98	1.93	0.80	0.60	1.07
Composite measure	0.81	0.41	1.60	0.20	0.12	0.34

Memory is a dichotomous variable with 1=score $\geq$ 20th percentile 0=score <20th percentile

Model 2: age, sex, race, memory, wave, southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), marital status (married, divorced/separated, widowed, never married), mother's and father's education (=<8 years, >8 years), height, height*sex interaction, log of household size-adjusted wealth, log of household size-adjusted income, and employment status (currently working for pay, not working for pay).

Table 8. Odds ratios for prediction of nursing home admission as a function of dementia risk, physical inactivity, alcohol use, and ever smoking (n=7631)

	Nursing Home Admission		
	OR	95%	CI
Low Dementia Probability	0.49	0.41	0.59
Low Physical Activity	1.27	1.15	1.41
No Alcohol Consumption	1.28	1.13	1.45
Heavy Alcohol Consumption	1.44	1.13	1.82
Ever Smoking	1.12	1.01	1.25

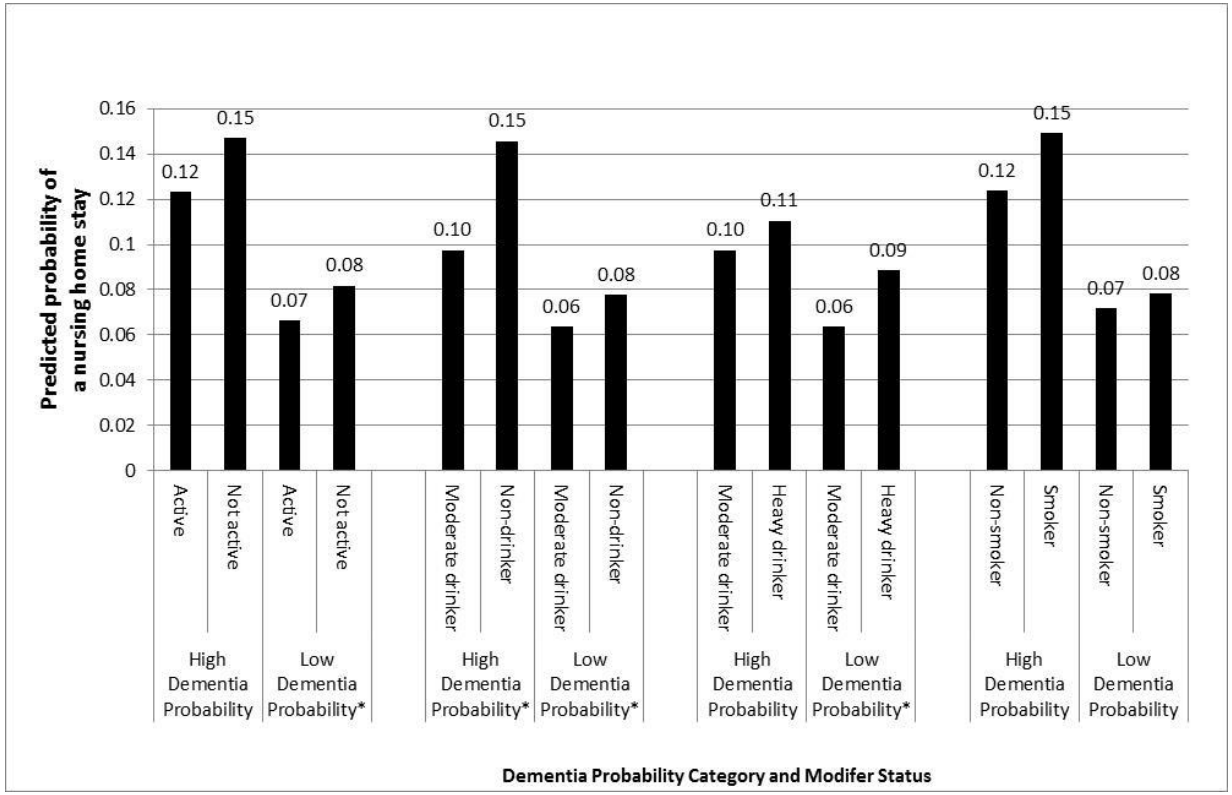
Note: Model is simultaneously adjusted for all of the risk factors.

Table 9. Association between dementia probability category and nursing home admission including interactions between dementia probability and each risk factor (n=7,631)

	Nursing Home Admission		
	OR	95%	CI
Physical Activity			
Low Dementia Probability	0.48	0.35	0.67
Low Dementia Probability*Low Physical Activity	1.02	0.70	1.47
Low Physical Activity	1.25	0.88	1.78
Alcohol Consumption			
Low Dementia Probability	0.61	0.38	0.98
Low Dementia Probability*No Alcohol Consumption	0.76	0.46	1.25
No Alcohol Consumption	1.65	1.02	2.66
Low Dementia Probability*Heavy Alcohol Consumption	1.25	0.42	3.72
Heavy Alcohol Consumption	1.17	0.40	3.38
Smoking			
Low Dementia Probability	0.52	0.41	0.67
Low Dementia Probability*Ever Smoking	0.87	0.63	1.20
Ever Smoking	1.27	0.94	1.72

Note: Models all include all of the other risk factors, but do not include interaction terms between the other risk factors and dementia probability. Interaction terms test the null that the relative effect of the risk factor is the same for individuals with high and low dementia probability.

Figure 1. Predicted probability of nursing home admission per wave, by modifier and dementia probability category.



Legend for Figure 1: Asterisks indicate a statistically significant difference in the predicted probability per wave of a nursing home admission for those with and without the modifier.

Families and Disability Onset: Are Spousal Resources Less Important for Individuals at High Risk of Dementia?

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Objective: *To determine whether social contacts and spousal characteristics predict incident instrumental or basic activities of daily living (I/ADL) limitations and whether effects differ for individuals with high risk of dementia.* **Design:** *Cohort study.* **Setting:** *Biennial interviews of Health and Retirement Study participants over up to 12 years.* **Participants:** *4,125 participants aged 65 years and older without baseline I/ADL limitations.* **Measurements:** *Participants' family characteristics (living arrangements, proximity to children, contacts with friends, marital status, and spouse's depression, employment, and education) and dementia probability (high versus low risk of dementia based on direct and proxy cognitive assessments) were characterized at baseline. Family characteristics and their interactions with dementia probability were used to predict incident I/ADL limitations in pooled logistic regressions.* **Results:** *ADL limitation incidence was higher among the unmarried (odds ratio [OR] versus married: 1.14; 95% CI: 1.01–1.30); those married to a depressed spouse (OR versus nondepressed spouse: 1.56, 95% CI: 1.21–2.00); or whose spouse had less than high school education (OR versus spouse with high school or more: 1.29, 95% CI: 1.06–1.57). Living with someone other than a spouse compared with living with a spouse predicted higher risk of both incident ADL (OR: 1.35; 95% CI: 1.11–1.65), and IADL (OR: 1.30; 95% CI: 1.06–1.61) limitations. Effects were similar for respondents with high and low dementia probability.* **Conclusions:** *Regardless of dementia risk, older adults may receive important marriage benefits, which help delay disability. The salience of spouse's education and depression status implicate modifiable mechanisms, such as information and instrumental support, which may be amenable to interventions.* (Am J Geriatr Psychiatry 2016; 24:585–594)

Key Words: disability, cognitive function, epidemiology, social ties

Social ties strongly predict many dimensions of health and disability, with hypothesized mechanisms involving the types of support provided by those ties. Various ties play distinct roles in the lives of older adults. For example, spouses and friends are thought to be key sources of emotional support, such as love

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http://dx.doi.org/10.1016/j.jagp.2016.02.003

and affection, and serve as confidantes. Children are more likely to provide instrumental support to aging parents, for example, helping with tasks such as grocery shopping or financial management.[1] Further, the importance of various ties appears to evolve with an individual's health, with some evidence that social support is more important for disease management than disease prevention.[2–5]

Previous research has observed that satisfactory subjective social support, and not network size, is associated with functional ability.[6] This suggests that it is not the number of social ties that may influence health outcomes, but characteristics of the ties. Characteristics of the individual providing support (e.g., depression, education, or employment) may shape their capacity to provide satisfactory support,[7] in particular to those who have memory impairment or incipient dementia. There is little empirical evidence, however, about how characteristics of the individual providing support influence care recipient outcomes. Examining the influence of network members on functional outcomes is important because some characteristics—for example, depression status or education—may be modifiable or highlight opportunities for intervention. These effects are particularly understudied for individuals with incipient dementia, and it is unclear whether network ties have similar benefits for individuals with cognitive impairments as for cognitively normal elderly.

We examined whether social ties and spousal characteristics predict onset of disability in older adults, and whether these patterns differed by dementia probability status. We hypothesized that being married, living with children or spouses, having weekly contact with friends, and having a spouse with at least a high school education, a spouse who was currently working, or a spouse who was not depressed would be associated with lower risk of incident instrumental or basic activity of daily living (I/ADL) limitations, even among cognitively impaired individuals.

METHODS

The Health and Retirement Study (HRS) is a nationally representative cohort of Americans aged 50 years or older and their spouse.[8,9] We restricted analyses to HRS participants who were aged 65 years or older in 1998 and followed these individuals biennially through 2010.

The HRS was approved by the University of Michigan Health Sciences human subjects committee. These analyses were determined to be exempt by the Harvard School of Public Health Office of Human Research Administration.

Outcome Assessment

We analyzed two dichotomous outcomes in separate models: any ADL limitation and any IADL limitation. During biennial interviews, participants or proxy respondents reported whether they had difficulty in the past 30 days in five ADLs (getting across a room, dressing, bathing, eating, and getting in and out of bed) and in five IADLs (using a phone, managing money, taking medication, shopping for groceries, and preparing hot meals). Participants reported "yes", "no", or "do not do" for each of these items. We used the RAND variables for any ADL limitation and any IADL limitation.[10] "Do not do" and "refused" are treated as missing in the RAND coding. A sensitivity analysis in which "do not do" and "refused" were treated as having a limitation found similar results to those reported here. Participants who reported any ADL or IADL limitations in 1998 or 2000 were excluded from our analyses.

Assessment of Resources and Risk Factors from Social Ties

The family-level variables examined in this study were living arrangements, proximity to children, contacts with friends, marital status, spouse's depression status, spouse's employment status, and spouse's education status. All exposure variables were assessed in 2000. For respondents missing information in 2000, we used 1998 values.

Living arrangements were classified as living with spouse (reference category), living with someone other than spouse, and living alone. Proximity to children was classified as living with children (reference category), having no children, living within 10 miles of children, living over 10 miles from children. Contact with friends was defined as at least weekly meetings with friends (reference category) versus less than weekly meetings with friends. Spouses of the HRS respondents are also included by the HRS sample design. All spousal characteristics were reported either by the spouse or by their proxy (except for depression) if the

spouse was unable to complete the questionnaire. Spouse's depression status was categorized as nondepressed spouse (reference category), depressed spouse, and no spouse. Spouse's depression was defined as reporting three or more depressive symptoms in the past 2 weeks, based on a modified eight-item Centers for Epidemiologic Studies-Depression (CES-D). Spouse's employment status was categorized as retired (reference category), working full-time, working part-time, not working or disabled, and no spouse. Spouse's education was classified as no high school degree; high school diploma or GED (reference category); bachelor's degree or higher; or no spouse. Marital status was defined as not married versus married. We also created a "social isolation index" similar to that used in previous studies,[11,12] in which people received one point for each of the following items: living alone, no children, or less than weekly contact with friends. The index ranged from 0 to 3 points.

Assessment of Dementia Risk

In addition to assessing family-level covariates in 2000, we also assessed cognitive function as measured by imputed dementia probability in 2000. The methods for calculating imputed dementia probability are described in detail elsewhere.[13] Briefly, the dementia probability score is calculated by combining direct and proxy-assessed cognitive status. These assessments were calibrated against a dementia diagnosis according to DSM-III-R and DSM-IV criteria in a subsample of HRS participants (C statistic: 94.3%). The dementia probability has a theoretical range from 0 (no chance individual has dementia) to 1 (individual certain to have dementia) and an actual range in our data of $4.38 \times e^{-13}$ to 0.99. We categorized dementia probability into two categories based on the 75th percentile in 2000 (cutpoint: 0.0178) and included this binary variable in all models.

Covariates

We controlled for a number of individual characteristics, demographics, health behaviors, and comorbidities. All of these potential confounders were assessed in 1998 (the wave prior to family-level variable assessment) and included age (centered, continuous), centered age squared (continuous), gender, race (black versus other), southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), mother's and father's education (≤8 years, >8 years), height (gender-specific baseline quartiles), and interview wave. We also performed sensitivity analyses in which we adjusted for all of the previously mentioned covariates plus log of household size-adjusted wealth (continuous), log of household size-adjusted income (continuous), body mass index (continuous), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), physical activity (active versus inactive), alcohol consumption (moderate versus nonmoderate drinking), current smoking (yes/no), depression (yes/no where yes was defined as reporting three or more depressive symptoms in the past 2 weeks, based on a modified eight-item CES-D). We adjusted for these additional covariates in sensitivity analyses because we hypothesized that many of these additional covariates could be confounders, but could also be mediators of the association between the family-level factors and risk of functional limitations. Participants missing any covariate in 1998 were excluded from all analyses.

Statistical Analyses

We estimated pooled logistic regression models using each social resource and risk factor to predict onset of any ADL limitation and, in separate models, onset of any IADL limitation. Pooled logistic regression approximates the Cox proportional hazards model when dealing with discrete time data and rare outcomes. For our ADL analyses, participants were censored from analyses after developing an ADL limitation, last interview, death, or the first wave of missing information on dementia probability or ADL limitations. We used a parallel approach for IADL analyses. We also performed sensitivity analyses stratified by gender. To test whether the effect of our family-level variables differed by cognitive status, we performed another set of analyses in which we included interactions between dichotomized high versus low dementia probability and each family-level variable in separate models for each variable. All analyses were performed using PROC SURVEYLOGISTIC in SAS 9.4 (SAS Institute, Cary, NC)

accounting for HRS sampling weights and repeated measures. We used t statistics to calculate p values.

RESULTS

Of the 10,367 participants aged 65 years or older in 1998, we excluded 3,850 people who either had an ADL or IADL limitation in 1998 or 2000; 722 people for whom information on I/ADL limitations were not available in 1998 or 2000; 578 people who did not answer the questions on I/ADL limitations in 2002; 350 people missing information on imputed dementia probability in 1998 or 2000; 428 people missing information on our family-level variables; and 314 people missing information on baseline covariates. Our final sample included 4,125 people.

Individuals with high dementia probability at baseline were less likely to be married compared with those with lower dementia probability (Table 1). During an

TABLE 1. Characteristics of those included in the analysis of dementia probability category and any incident I/ADL limitation by dementia probability category at first exposure wave

Characteristic	High Dementia Probability (N = 1032)	Low Dementia Probability (N = 3093)
Age (mean, std)	76.1 (6.3)	71.5 (5.2)
Gender (% male)	56.4	39.1
Race (% black)	14.5	7.5
Southern birthplace (%)	15.8	12.3
Years of education (mean, std)	11.3 (3.2)	13.0 (2.6)
Mother had ≥8 years of education (%)	44.5	55.0
Father had ≥8 years of education (%)	39.9	47.1
Physically inactive (%)	54.8	48.5
Not drinking moderately (%)	78.8	71.2
Current smoker (%)	10.3	9.0
Current depression (%)	10.3	7.4
Body mass index (mean, std)	25.8 (4.0)	26.2 (4.3)
Number of comorbidities (mean, std)	1.6 (1.2)	1.5 (1.1)
Living arrangement		
Live with spouse	55.0	62.7
Live with someone other than spouse	11.1	8.4
Live alone	33.9	28.9
Proximity to children		
Live with children	16.6	14.7
No children	7.6	7.5
Children within 10 miles	46.6	44.2
Children over 10 miles	29.3	33.6
Less than weekly contact with friends	37.7	39.1
Spouse's employment status		
Retired	34.8	39.5
Full time	2.1	4.2
Part time	6.5	10.3
Not working/disabled	11.6	8.7
No spouse	45.0	37.3
Spouse's depression status		
Not depressed	48.3	58.2
Depressed	6.8	4.5
No spouse	45.0	37.3
Spouse's educational status		
High school diploma/GED	36.1	37.2
College diploma or higher	6.8	14.9
Less than a high school diploma/GED	12.3	10.6
No spouse	44.9	37.3
Isolation index		
Not isolated	38.4	39.8
Isolated (1 point)	45.5	46.2
Isolated (2 points)	15.5	12.8
Isolated (3 points)	0.9	1.2
Marital status		
Not married	44.9	37.3
Married	55.1	62.7

TABLE 2. Association between family-level variables and risk of incident ADL and IADL limitations

	ADL					IADL				
	OR	95%	CI	t statistic	p value[a]	OR	95%	CI	t statistic	p value[a]
Marital status										
Married	1.00	ref				1.00	ref			
Not married	1.14	1.01	1.30	2.04	0.05	1.04	0.92	1.18	0.65	0.52
Living arrangement										
Live with spouse	1.00	ref				1.00	ref			
Live with someone other than spouse	1.35	1.11	1.65	2.95	0.01	1.30	1.06	1.61	2.47	0.02
Live Alone	1.10	0.96	1.25	1.36	0.18	0.99	0.87	1.13	−0.12	0.91
Proximity to children										
Live with children	1.00	ref				1.00	ref			
No children	0.95	0.75	1.22	−0.38	0.71	0.79	0.62	1.01	−1.86	0.07
Children within 10 miles	0.89	0.75	1.05	−1.44	0.16	0.93	0.79	1.11	−0.79	0.44
Children over 10 miles	0.87	0.73	1.04	−1.51	0.13	0.87	0.73	1.04	−1.55	0.13
Contacts with friends										
Weekly or more frequent contact	1.00	ref				1.00	Ref			
Less than weekly contact	1.03	0.92	1.15	0.43	0.67	1.06	0.95	1.19	1.00	0.32
Spouse's employment status										
Retired spouse	1.00	ref				1.00	ref			
Spouse employed full time	0.92	0.64	1.33	−0.43	0.67	0.79	0.54	1.17	−1.18	0.24
Spouse employed part time	0.98	0.79	1.22	−0.17	0.87	0.93	0.75	1.17	−0.62	0.54
Spouse not working	1.06	0.86	1.32	0.55	0.59	0.92	0.73	1.15	−0.77	0.45
No spouse	1.14	1.00	1.31	1.97	0.05	1.01	0.89	1.16	0.19	0.86
Spouse's depression status										
Not depressed spouse	1.00	ref				1.00	ref			
Depressed spouse	1.56	1.21	2.00	3.47	<0.01	1.23	0.93	1.63	1.48	0.14
No spouse	1.19	1.05	1.35	2.64	0.01	1.06	0.93	1.20	0.87	0.39
Spouse's educational status										
Spouse with less than high school education	1.29	1.06	1.57	2.54	0.02	0.83	0.68	1.01	−1.85	0.07
Spouse with high school education	1.00	ref				1.00	Ref			
Spouse with college education	1.03	0.84	1.26	0.29	0.78	0.98	0.80	1.21	−0.17	0.87
No spouse	1.23	1.06	1.43	2.74	0.01	0.99	0.86	1.14	−0.16	0.88
Isolation index										
Not isolated	1.00	ref				1.00	ref			
Isolated (1 point)	1.06	0.94	1.20	0.92	0.36	0.97	0.86	1.10	−0.43	0.67
Isolated (2 points)	1.07	0.90	1.27	0.74	0.46	1.00	0.84	1.18	−0.04	0.97
Isolated (3 points)	0.97	0.63	1.47	−0.16	0.87	0.74	0.42	1.30	−1.04	0.30

Notes: Adjusted for age, gender, race, southern birthplace, years of education, mother's and father's education, height, and interview wave.
[a]4,124 degrees of freedom; p values have been rounded up to the nearest hundredths place.

average of 7 years of follow-up, 1,528 people reported developing an ADL limitation and 1,523 people reported developing an IADL limitation.

As expected, low dementia probability was associated with lower risk of both ADL (OR: 0.76; 95% CI: 0.66–0.87) and IADL limitations (OR: 0.55; 95% CI: 0.48–0.63) (results not shown in tables). Proximity to children, frequency of contacts with friends, spouse's employment status, and the isolation index were not significantly associated with the risk of incident ADL or IADL limitations (Table 2). Being unmarried compared with being married was associated with increased risk of incident ADL limitations but not IADL limitations (Table 2). Using a 2-year risk of ADL disability of 11.3% for married individuals compared with 10.1% for non-married individuals and assuming a constant rate over time, this translates to a median time of onset of ADL limitations of 13.7 years compared with 12.2 years for those without a depressed spouse (see Supplement 1). Living with someone other than a spouse compared with living with a spouse was associated with an increased risk of both ADL and IADL limitations (Table 2) and a 3.0-year decrease in the median time to onset of ADL limitations. Having a depressed spouse compared with a nondepressed spouse was significantly associated with higher risk of incident ADL limitations, corresponding to a 4.1-year decrease in the median time to

onset of ADL limitations (Table 2). Additionally, having a spouse with less than high school education compared with a spouse with a high school diploma was associated with increased risk of incident ADL limitations, corresponding to a 2.5-year shorter median time to onset of ADL limitations (Table 2).

When we adjusted for potential mediating variables in a sensitivity analysis, the point estimates for the association between marital status or living with someone other than a spouse and risk of ADLs were attenuated and no longer statistically significant. This suggests that that effects of being married or living with someone other than a spouse may be partially mediated by these factors.

Among men, having a depressed spouse was associated with an increased risk of ADL limitations (OR: 1.66; 95% CI: 1.22–2.28) and having a spouse with less than a high school education was also associated with an increased risk of ADL limitations (OR: 1.44; 95% CI: 1.08–1.92). These associations were not observed among women (Supplemental Tables S3 and S4).

We also evaluated whether the association between our family level values and incident I/ADL limitations varied by cognitive status. Low dementia probability was associated with lower risk of incident ADL and ADL limitations in almost all models. We found no significant interactions between our family-level variables and dementia probability status and all interaction terms were close to null (Table 3); in other words, the estimated impact of family-level variables was not statistically distinguishable for individuals with high and low dementia probability.

DISCUSSION

After controlling for demographics and cognitive status, we found that not being married, living with someone other than a spouse, having a depressed spouse, or having a spouse with less than a high school education predicted higher risk of incident ADL limitations. Although they did not reach statistical significance, results for IADLs are similar to those seen for ADLs, with the exception of spouse's education. Contrary to our hypotheses, other family-level variables were not significantly associated with incident I/ADL limitations. We did not observe any significant interactions between cognitive status and our family-level variables. Although we found no evidence that family level variables had larger or smaller effects for people at high risk of dementia, this does not prove effects are identical; given our confidence intervals, most results were consistent with modest differences in either direction.

Previous literature on marital status or living with a spouse and incident disability has shown varying results.[14–17] The larger size and longer follow-up time of our study compared with the majority of these previous studies increased our ability to examine the long-term effects of marriage on functional limitations among the elderly. Additionally, we were able to examine both IADLs and ADLs. Only one previous study among women followed for 2 years examined both ADLs and IADLs.[15] One reason for the varying results among studies may be because these are different pathways through which marital status may impact disability. Whereas emotional support may improve physical functioning and disability, some types of support, particularly instrumental support, may lead to greater disability.[16] This suggests that social support may act on incident limitations through a variety of pathways, some of which may have beneficial effects while others may have harmful effects.

We found that spousal characteristics (particularly depression, employment status, and educational attainment) may impact the onset of disability. This finding suggests that an individual may influence their spouse's disability via active problem-solving strategies, such as environmental modifications to improve accessibility, by directly helping the individual complete the activity, or by promoting and sustaining healthy behavioral patterns (e.g., physical activity or adherence to medical advice). In our study, spouse's depression was associated with a higher prevalence of physical inactivity and depression in the respondent (see Supplement 5), which are risk factors for disability.[18–20] We hypothesized that spousal characteristics such as depression, employment, and education could influence the spouse's capacity to provide meaningful support. For example, depressed spouses may have less energy and motivation to problem-solve for disability prevention, and spouse's education may influence the spouse's access to relevant information regarding environmental modifications that could prevent disability. The quality and type of support provided may then impact the onset of IADL and ADL disability. In this sample, having a depressed spouse

TABLE 3. Association between dementia probability and incident I/ADL limitations including interactions between dementia probability and family-level variables

	ADL					IADL				
	OR	95%	CI	t statistic	p values[a]	OR	95%	CI	t statistic	p values[a]
Marital status										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.77	0.64	0.92	−2.90	0.01	0.55	0.46	0.66	−6.60	<.01
Not married	1.00	ref				1.00	ref			
Married	1.16	0.92	1.45	1.26	0.21	1.04	0.83	1.29	0.33	0.75
Married*Low dementia probability	0.98	0.76	1.26	−0.16	0.88	1.01	0.79	1.29	0.06	0.95
Living arrangement										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.77	0.64	0.92	−2.86	<0.01	0.55	0.46	0.66	−6.57	<0.01
Live with spouse	1.00	ref				1.00	ref			
Live with someone other than spouse	1.22	0.83	1.78	1.02	0.31	1.24	0.86	1.77	1.15	0.25
Low dementia probability*Live with someone other than spouse	1.17	0.76	1.79	0.70	0.49	1.08	0.71	1.64	0.35	0.73
Live alone	1.16	0.91	1.47	1.21	0.23	1.00	0.80	1.27	0.03	0.98
Low dementia probability*Live alone	0.92	0.71	1.21	−0.58	0.56	0.98	0.75	1.28	−0.14	0.89
Proximity to children										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.71	0.51	0.98	−2.09	0.04	0.61	0.45	0.84	−3.07	<0.01
Live with children	1.00	ref				1.00	ref			
No children	0.70	0.45	1.11	−1.52	0.13	0.72	0.47	1.10	−1.51	0.14
Low dementia probability*No children	1.55	0.91	2.64	1.62	0.11	1.15	0.69	1.93	0.55	0.59
Children within 10 miles	0.89	0.65	1.21	−0.77	0.45	1.00	0.74	1.33	−0.03	0.98
Low dementia probability*Children within 10 miles	1.00	0.70	1.43	−0.01	1.00	0.91	0.64	1.29	−0.54	0.59
Children over 10 miles	0.80	0.57	1.12	−1.30	0.20	1.00	0.73	1.38	0.00	1.00
Low dementia probability*Children over 10 miles	1.13	0.77	1.67	0.62	0.54	0.81	0.55	1.19	−1.08	0.28
Contacts with friends										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.77	0.65	0.91	−3.06	<0.01	0.55	0.47	0.66	−6.93	<.01
Weekly or more frequent contact	1.00	ref				1.00	ref			
Less than weekly contact	1.04	0.84	1.29	0.35	0.73	1.06	0.86	1.31	0.57	0.57
Low dementia probability*Less than weekly contact	0.98	0.76	1.26	−0.15	0.88	1.00	0.78	1.28	−0.04	0.97
Spouse's employment status										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.83	0.67	1.04	−1.61	0.11	0.54	0.44	0.67	−5.73	<.01
Retired spouse	1.00	ref				1.00	ref			
Spouse employed full time	0.46	0.14	1.53	−1.26	0.21	1.24	0.58	2.69	0.55	0.58
Low dementia probability*Spouse employed full time	2.15	0.61	7.55	1.20	0.23	0.57	0.23	1.38	−1.25	0.21
Spouse employed part time	1.34	0.87	2.04	1.34	0.19	0.74	0.46	1.19	−1.23	0.22
Low dementia probability*Spouse employed part time	0.67	0.41	1.10	−1.59	0.12	1.35	0.79	2.30	1.08	0.28
Spouse not working	1.29	0.91	1.83	1.42	0.16	0.90	0.63	1.30	−0.55	0.59
Low dementia probability*Spouse not working	0.74	0.48	1.15	−1.32	0.19	1.02	0.65	1.59	0.07	0.95
No spouse	1.23	0.96	1.59	1.63	0.11	0.99	0.78	1.25	−0.10	0.92
Low dementia probability*No spouse	0.90	0.68	1.20	−0.70	0.49	1.04	0.79	1.36	0.27	0.79
Spouse's depression status										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.76	0.63	0.92	−2.79	0.01	0.54	0.45	0.65	−6.50	<.01
Not depressed spouse	1.00	ref				1.00	ref			
Depressed spouse	1.42	0.92	2.18	1.59	0.12	1.11	0.69	1.79	0.45	0.66
Low dementia probability*Depressed spouse	1.16	0.68	1.97	0.55	0.59	1.18	0.66	2.11	0.57	0.58
No spouse	1.20	0.95	1.52	1.53	0.13	1.04	0.83	1.30	0.33	0.75
Low dementia probability*No spouse	0.99	0.76	1.28	−0.10	0.93	1.03	0.80	1.32	0.21	0.84
Spouse's educational status										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.82	0.66	1.03	−1.69	0.09	0.59	0.48	0.73	−4.85	<.01
Spouse with less than high school education	1.49	1.05	2.11	2.22	0.03	0.93	0.66	1.31	−0.43	0.67
Low dementia probability*Spouse with less than high school education	0.82	0.54	1.23	−0.97	0.34	0.84	0.55	1.27	−0.83	0.41

(*Continued*)

TABLE 3. (*Continued*)

	ADL					IADL				
	OR	95%	CI	t statistic	p values[a]	OR	95%	CI	t statistic	p values[a]
Spouse with high school education	1.00	ref				1.00	ref			
Spouse with college education	1.18	0.75	1.84	0.71	0.48	1.15	0.73	1.82	0.62	0.54
Low dementia probability*Spouse with college education	0.84	0.52	1.38	−0.68	0.50	0.81	0.49	1.33	−0.82	0.41
No spouse	1.32	1.02	1.71	2.13	0.04	1.02	0.80	1.31	0.19	0.85
Low dementia probability*No spouse	0.90	0.68	1.20	−0.72	0.48	0.95	0.72	1.25	−0.38	0.71
Isolation index										
High dementia probability	1.00	ref				1.00	ref			
Low dementia probability	0.78	0.63	0.98	−2.19	0.03	0.54	0.44	0.67	−5.76	<.01
Isolation (1 pt)	1.13	0.90	1.43	1.04	0.30	0.96	0.76	1.20	−0.38	0.71
Isolation (1 pt)*Low dementia probability	0.91	0.69	1.19	−0.68	0.50	1.02	0.79	1.34	0.18	0.86
Isolation (2 pts)	1.01	0.73	1.40	0.07	0.95	0.93	0.69	1.27	−0.45	0.66
Isolation (2 pts)*Low dementia probability	1.09	0.75	1.58	0.43	0.67	1.11	0.77	1.59	0.56	0.58
Isolation (3 pts)	1.02	0.56	1.85	0.06	0.95	0.83	0.28	2.44	−0.34	0.74
Isolation (3 pts)*Low dementia probability	0.93	0.41	2.07	−0.19	0.85	0.85	0.24	3.05	−0.24	0.81

Notes: Adjusted for age, gender, race, southern birthplace, years of education, mother's and father's education, height, and interview wave.
[a]4124 degrees of freedom; p-values have been rounded up to the nearest hundredths place.

increased the risk of ADL limitations, and this effect was similar regardless of dementia probability status. Previous research has also suggested that depressive symptoms in one spouse may affect the physical health of the other spouse. In the Assets and Health Dynamics Among the Oldest Old (AHEAD) study, researchers found that elevated depressive symptoms in one spouse predicted increases in functional limitations in the corresponding partner.[21] The earliest birth cohorts in the current analyses include participants in AHEAD. Our study expands upon this previous research by including more recent birth cohorts, examining the association between depressive symptoms at baseline and new onset of functional limitations, and assessing whether associations differed by cognitive status. The importance of spouse's depression has also been documented in other patient populations—for example, in a study of patients with rheumatoid arthritis, spousal depression was associated with increased patient disability and disease activity.[22] Interestingly, a later study found that spouse's depression significantly predicted function limitations only when the patient perceived a low empathic response in the spouse, implicating pathways related to emotional support rather than our hypothesized instrumental and informational support mechanisms.[23]

Having a spouse with low education also appeared to increase risk of ADL limitations. Previous research demonstrates that lower spousal education correlated with increased risk of mortality and poor health and health behaviors.[24–26] It is difficult, however, to determine if the effect of spouse's education on these outcomes is causal. Additionally, unlike the other spousal characteristics, which had similar directions of associations for both ADLs and IADLs, we are unsure why having a spouse with low education did not increase the risk of IADL limitations.

Differences between the results of this study and previous studies on the impact of family-level characteristics on incident I/ADL limitations may be explained by some of the differences in the design of our study compared with previous analyses. First, we were unable to determine the specific types of support (instrumental versus emotional) provided by spouses, children, or friends. Because emotional support may help to protect against disability whereas instrumental support can increase the risk of disability in certain situations, our lack of detailed information on support or types of support may explain why we did not see strong effects for contacts with children or friends on incident I/ADL limitations.

A few limitations to our study should be noted. We were unable to determine if the impact of our spousal characteristics on incident ADL limitations is due to causal effects or confounding. Also, spouse's assistance with an activity may lead to under-reporting of limitations. The respondents may report no limitation, but, in reality, without their spouse's help, they

would experience difficulty completing the activity. Additionally, we did not consider the order in which I/ADL limitations occurred, the co-occurrence of both ADL and IADL limitations, back-transitions due to the resolution of I/ADL limitations, or the severity of the reported I/ADL limitations. We also did not examine changes in the family-level characteristics over time and only tested a limited number of spousal and family-level characteristics. Finally, some of our effects would not meet a Bonferroni-corrected significance threshold.

Strengths to our study include the use of a large, nationally representative cohort. The longitudinal nature of this study allowed us to assess family-level variables and cognitive status prior to the onset of I/ADL limitations. We were also able to control for a variety of confounders at the individual level. Additionally, the use of imputed dementia probability categories allowed us to retain even severely cognitively impaired individuals in our analyses. We were also able to explore whether the influence of these family-level factors varied based on the individual's cognitive function—a topic that many previous studies did not explore. Finally, we evaluated the impact of family-level variables on ADL and IADL limitations separately, and found distinct patterns for these two categories of limitations.

Results from this study suggest that not being married, living with someone other than your spouse, and spouse's depression status and educational status may influence the onset of ADL limitations in the other spouse regardless of their level of cognitive impairment. This suggests that the characteristics of the spouse may influence their ability to provide the type of support needed to avoid incident ADL limitations. It is not clear in our study whether spouses are so important specifically because they provide care in the context of illness or because they provide less structured routine support. Most prior research focuses on the role of spouses as caregivers once their loved one has a diagnosed condition or need (e.g., dementia). For example, previous research indicates that interventions with spousal caregivers can have important benefits for the care recipient.[27] Depressive symptoms are common in spousal caregivers[28] and our findings suggest that treating such depression may help both spouses. It is also possible that spouses influence onset of I/ADL limitations in the absence of diagnosed conditions by promoting healthful daily routines such as physical activity. For example, spousal support improves effectiveness of physical activity interventions.[29] Spouses may also impact the use of healthcare resources. For example, there is evidence that married individuals use higher quality hospitals and have shorter lengths of stay than those who are widowed.[30] Spouse's education may further influence their ability to access the resources (for example, healthcare or adaptive equipment) that their partner needs to prevent the onset of I/ADL limitations. Education is associated with health literacy[31] and increasing health literacy has been positively associated with knowledge of health services and health outcomes.[32,33] This suggests that low education spouses may have lower health literacy and may have difficulty accessing the health resources needed by their spouse to remain independent.

These results highlight the importance of spousal relationships in healthy aging, and the potential influence of interventions delivering support and resources to spouses of vulnerable elderly individuals. By providing support to a spouse, we may be able to reduce the risk of ADL limitations in their partner. Although some family-level factors are not amenable to interventions, some of the spousal characteristics may provide opportunities for design or targeting of interventions. By providing spouses with mental health resources or understanding what resources are not reaching low education spouses, we may be able to improve their ability to help their spouse develop coping strategies or use adaptive equipment to avoid the onset of functional limitations.

This work was supported by the Telemedicine and Advanced Technology Research Center (TATRC) at the U.S. Army Medical Research and Materiel Command (USAMRMC) through award W81XWH-12-1-0143.

The authors have no disclosures to report.

APPENDIX: SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at doi:10.1016/j.jagp.2016.02.003.

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Published in final edited form as:
J Alzheimers Dis. 2015 January 1; 44(4): 1171–1180. doi:10.3233/JAD-141866.

Do Physical Activity, Smoking, Drinking, or Depression Modify Transitions from Cognitive Impairment to Functional Disability?

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Abstract

BACKGROUND—Individual-level modifiers can delay onset of limitations in basic activities of daily living (ADLs) among cognitively impaired individuals. We assessed whether these modifiers also delayed onset of limitations in instrumental ADLs (IADLs) among individuals at elevated dementia risk.

OBJECTIVES—To determine whether modifiable individual-level factors delay incident IADL limitations among adults stratified by dementia risk.

METHODS—Health and Retirement Study participants aged 65+ without activity limitations in 1998 or 2000 (N=5,219) were interviewed biennially through 2010. Dementia probability, categorized in quartiles, was used to predict incident IADL limitations with Poisson regression. We estimated relative (risk ratio) and absolute (number of limitations) effects from models including dementia, individual-level modifiers (physical inactivity, smoking, no alcohol consumption, and depression) and interaction terms between dementia and individual-level modifiers.

RESULTS—Dementia probability quartile predicted incident IADL limitations (relative risk for highest versus lowest quartile=0.44; 95% CI: 0.28–0.70). Most modifiers did not significantly increase risk of IADL limitations among the cognitively impaired. Physical inactivity (RR=1.60; 95% CI: 1.16, 2.19) increased the risk of IADL limitations among the cognitively impaired. The interaction between physical inactivity and low dementia probability was statistically significant

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(p=0.009) indicating that physical inactivity had significantly larger effects on incident IADLs among cognitively normal than among those with high dementia probability.

CONCLUSION—Physical activity may protect against IADL limitations while smoking, alcohol consumption and depression do not afford substantial protection among the cognitively impaired. Results highlight the need for extra support for IADLs among individuals with cognitive losses.

Keywords

epidemiology; cognition; disability

INTRODUCTION

Limitations in instrumental activities of daily living (IADLs) increase caregiver burden and risk of institutionalization.[1, 2] Cognitive impairment both increases the risk of incident IADL limitations[3] and exacerbates the financial and caregiver burden associated with such limitations.[4, 5] Several individual behaviors and resources are known to influence the onset of disability in cognitively healthy older adults[6–10], but it is not known whether these modifiable factors have similar effects for individuals with cognitive impairments.[11]

In a previous study, we reported that the impact of cognitive impairment on the risk of incident limitations in *basic* activities of daily living (ADLs), such as independent dressing and bathing, is substantially reduced by modifiable factors including not smoking and moderate alcohol consumption.[12] However, because IADLs are generally more cognitively demanding than ADLs[13], individual-level factors may not prevent IADL limitations among those with cognitive impairment.[14] In other words, ADLs tend to be defined by physical capacities, for which individual-level modifiers like smoking have clear relevance (such as decreased lung capacity). The link to such individual-level modifiers may or may not hold for IADLs, because the skills involved in IADLs pertain more directly to facilities of logic, thought, or reasoning. Sustaining healthy behaviors is challenging for everyone and may present even larger burdens for individuals with cognitive impairments and their caregivers. As a result, it is extremely valuable for clinicians and families to understand the potential benefits of improved risk profiles. Clinicians and families can then focus their efforts on those modifiers which may have the greatest impact on the patient's function and understand what types of benefits are feasible. Additionally, if these individual-level factors do not exhibit strong effects on incident IADL limitations, this will suggest that clinicians and families may need to provide direct support for IADLs.

Using data from the Health and Retirement Study (HRS), we expanded upon our previous research to examine whether four individual-level factors–low physical activity, not consuming alcohol, smoking, and depression–were associated with incident IADL limitations regardless of cognitive function; in other words, do these factors have benefit among those with cognitive impairment or are they relevant for the onset of IADL limitations only among those with high cognitive function? We focused on these factors because, unlike demographic characteristics like age or gender, these factors can be modified or treated. Given the cognitive demands of most IADL tasks, we hypothesized that

these individual-level factors would have large benefits for individuals with low dementia probability, but fewer benefits for individuals with high dementia probability.

MATERIALS AND METHODS

HRS has been described in detail previously.[15, 16] In brief, this is a nationally representative cohort of Americans aged 50 years or older and their spouses. We restricted our analyses to those participants enrolled in HRS and aged 65 years or older in 1998; we use data from biennial follow-ups through 2010.

HRS was approved by the University of Michigan Health Sciences Human Subjects Committee. These analyses were determined to be exempt by the Harvard School of Public Health Office of Human Research Administration.

Outcome Assessment

During the biennial interviews, participants were asked to report if they had difficulty in five IADLs in the past 30 days. These activities included using a phone, managing money, taking medication, shopping for groceries, and preparing hot meals, items selected from the Lawton and Brody index.[17] Development and validation of these items is described in more detail in HRS documentation[18] and subsequent research. For example, all items were shown to predict two-year mortality in a subsample of HRS.[19] Participants reported “yes,” “no” or “do not do” to each of these items. For consistency with prior work, we used the RAND variable for any activity limitation,[20] which sums reported activity limitations in the five IADLs and ranges from 0 to 5. “Don’t do” and “refused” are treated as no limitation in the RAND coding. Those who reported any activity limitations in 1998 or 2000 were excluded from our analyses, so we could evaluate predictors of incident limitations. Sensitivity analyses indicated results were similar when respondents were censored at first report of “don’t do” or “refused” for any item and when the food preparation and managing money items were excluded from the outcome definition.

Exposure Assessment

We used imputed dementia probability as our measure of cognitive functioning in this study. Methods for calculating this score have been described in detail elsewhere.[21] In brief, participants able to complete cognitive interviews were assessed via immediate and delayed recall of a 10-word list and a modified Telephone Interview for Cognitive Status. If a participant was too impaired to participate in cognitive interviews, proxies completed the Jorm Informant Questionnaire for Cognitive Decline[22–24] and a single item memory impairment question. Additionally, a subset of HRS participants completed a multi-instrument memory assessment. To impute dementia probabilities, the proxy and participant assessments were combined and calibrated against dementia diagnosis according to DSM-III-R and DSM-IV criteria (C statistic = 94.3%). The dementia probability has a theoretical range from 0 (no chance individual has dementia) to 1 (individual certain to have dementia) and an actual range in our data of $4.38*e^{-13}$ to 0.99.

For the purpose of these analyses, the dementia probabilities were divided into four categories based on the quartile cutpoints of the dementia probability distribution in the first

exposure wave (2000). The reference group for all analyses was the highest dementia probability quartile. The other dementia categories were modeled as three indicator variables and interactions between modifiers and each indicator variable were used to test whether effects differed by dementia probability. In all analyses, dementia probability was assessed in the wave prior to IADL assessment. We also performed sensitivity analyses in which participants were categorized into two groups based on a cutpoint of the 90th percentile of the dementia probability distribution at baseline. The effects of our modifiers were similar to those seen in our main analyses (see supplemental material).

Assessment of Individual Level Modifiers

We assessed whether physical inactivity, not consuming alcohol, smoking, or depression accelerated onset of IADL limitations among individuals in the highest dementia probability category. We slightly modified the RAND version[20] of these variables to account for changes in questions over time and to create dichotomous variables consistent with our previous work.[12, 25] We dichotomized physical activity as active versus inactive. Since the questions on physical activity changed over time, in 1998, 2000, and 2002, we defined "active" as vigorous activity 3 or more times per week. From 2004 onwards, we defined active as vigorous activity 1 or more times per week. Although this is a lower level of physical activity, this category was the closest to the category used in earlier questionnaires. We dichotomized alcohol consumption as moderate drinking (more than zero and fewer than two drinks per day) versus not drinking. Due to the small number of heavy drinkers (2 or more drinks per day) in this cohort, we were not able to examine interactions between heavy drinking and dementia probability and excluded heavy drinkers from our analyses of alcohol consumption. To calculate drinks per day, the number of drinks consumed on days the participant drinks was multiplied by the number of days per week the participant reported drinking and the result was divided by seven. Current smoking status was a binary variable (yes/no). We dichotomized depressive symptoms as depressed versus not depressed, defined as reporting three or more depressive symptoms in the past two weeks using a modified 8-item Centers for Epidemiologic Studies-Depression scale. All modifiers were assessed in the wave prior to outcome assessment.

Covariates

We adjusted for both time-constant and time-varying confounders. Our time-constant confounders were assessed in 1998 and included: age (centered, continuous), centered age squared (continuous), gender, race (black versus other), southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), mother's and father's education (=<8 years, >8 years), and height (gender-specific baseline quartiles). Our time-varying confounders were all assessed in the wave prior to the exposure and included: marital status (divorced/separated, widowed, never married, married), log of household size-adjusted wealth (continuous), body mass index (continuous), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), low income (dichotomized using a cutpoint of $12,031, the 25th percentile of household-size adjusted income at baseline), our individual level modifiers, and interview wave. Participants missing any covariate at baseline were excluded from all

analyses. If a covariate or modifier value was missing during follow-up, we carried forward the last known value of the covariate or modifier.

Statistical Analysis

Our outcome was the count of IADL limitations at each wave which allowed us to model the total number of limitations experienced by an individual. Poisson regression models were used to estimate the relative risk of reporting IADL limitations for each dementia probability category. Participants were censored from analyses after developing any IADL limitation, last interview, death, or at the first wave of missing information on dementia probability or IADL limitations.

We used two approaches to determine if the individual-level factors had differential effects on the risk of incident IADL limitations for participants in each of the dementia categories. First, we included an interaction term between each dementia category and each modifier (in separate models for each modifier). This tests whether the modifier has different *relative* effects on the development of IADL limitations depending upon the participant's dementia probability. To correct for overdispersion and clustering, we used sandwich variance estimators.[26] These analyses were performed using PROC GENMOD in SAS 9.3 using the covb option and with weights described below.

Second, using the "margins" command in Stata 12, we computed the expected number of IADL limitations if everyone in the population was in the low, mild, moderate, or high dementia probability categories and had either the "beneficial" or "adverse" value of the modifier. This estimates the *absolute* effect of each modifier for each dementia probability category. The average number of expected incident IADL limitations was calculated using coefficients estimated in Poisson regression models with interaction terms and the actual population distribution of other covariates.

We used inverse probability weights (IPWs) to account for time-varying confounders, selective survival, and attrition.[27] The IPWs use lagged covariate values, so our first "exposure" wave was 2000 and our first "outcome" wave was 2002. We constructed weights for dementia probability category, modifier status, survival and participation in HRS. The weights and the HRS sampling weight from 1998 were multiplied together to create a final weight for each participant; the final weight reflects the inverse of the probability that the individual was alive and participated in the outcome wave and had the dementia category and modifier values he or she actually had, given his or her past dementia probability, modifier and covariate history. Weights were stabilized[27] and truncated at the 98th percentile to minimize outlier influence.

We used identical methods to those describe above for sensitivity analyses with the alternative operationalization of the exposure (cutpoint at the 90th percentile of the dementia probability distribution at baseline). Due to concerns that some IADL instructions may be gender specific, we also performed additional sensitivity analyses excluding managing money and preparing hot meals and found similar results to those shown here (not shown).

From the 10,367 individuals aged 65 or older in 1998, we excluded the 3391 participants who reported prevalent IADL limitations in 1998 or 2000 or who did not answer any of the questions on IADL limitations in 1998. We also excluded 747 participants who did not answer the question on IADL limitations in 2002 and 453 participants for whom cognitive measures were not available in 1998 or 2000. Finally, we excluded 355 participants missing baseline covariate information, leaving 5219 participants for our analyses.

RESULTS

Among respondents with the highest probability of dementia at baseline, 63.% were physically inactive, 77.7% did not consume alcohol and 13.6% were depressed. In comparison, among respondents with low dementia probability 48.1% were physically inactive, 69.4% did not consume alcohol and 8.1% were depressed (Table 1). Individuals with the highest probability of dementia reported the highest mean number of limitations at each wave (Table 2).

The low dementia probability category was associated with lower risk of incident IADL limitations (relative risk=0.44, 95% CI: 0.28–0.70). Compared to high dementia probability, mild (relative risk=0.35; 95% CI: 0.27–0.45) and moderate probability of dementia (relative risk=0.53; 95% CI: 0.44–0.65) were also associated with significantly lower risk of incident IADL limitations (results not shown in tables). Physical inactivity (relative risk=1.50; 95% CI: 1.20, 1.87) significantly predicted a higher risk of incident IADL limitations. The association between depression and incident IADL limitations did not reach conventional thresholds for statistical significance but suggested a harmful effect (relative risk=1.29; 95% CI: 0.99, 1.69, p-value =0.06).

Table 3 shows the association between our dementia probability categories and the risk of incident IADL limitations, the association between each modifier and incident IADL limitations, and the interaction between each dementia probability category and each modifier. In these models, an interaction coefficient of 1 indicates the modifier has the same relative effect on IADL limitations in those with high dementia probability as in those with low dementia probability. If the interaction coefficient is less than 1, it indicates the modifier effect is lower (less harmful) among those with low dementia probability; conversely, if the interaction coefficient is greater than 1, it indicates the modifier effect is higher (more harmful) among those with low dementia probability.

Physical inactivity predicted higher increased risk of incident IADL limitations among those with high dementia probability (RR=1.60; 95% CI: 1.16, 2.19). The interaction between physical inactivity and low dementia probability was over 1 and statistically significant (RR=2.28, 95% CI: 1.05, 4.93) indicating that the estimated relative harm of physical inactivity is greater among those with the lowest dementia probability than among those with the highest probability of dementia.

The three other modifiers we examined – not consuming alcohol, smoking, and depression – were not significantly associated with increased risk of IADL limitations among those with high dementia probability. The interaction terms between these modifiers and most of our

dementia categories were not statistically significant, so there was also no evidence that the relative harm of these modifiers differed by dementia probability. Although the interaction between the moderate dementia probability and depression was statistically significant (RR=1.81, 95% CI: 1.03, 3.17), the effect was not seen for other dementia probability categories and showed no consistent pattern across levels of dementia probability.

We also estimated the absolute impact of the modifiers on the risk of incident IADL limitations for individuals in different dementia categories, by calculating predicted number of incident IADL limitations in each group. Respondents in the high dementia probability category who were physically active were predicted to develop an average of 0.25 incident IADL limitations over the next two years (Figure 1). Those in the high dementia probability category who were physically inactive were expected to develop 0.39 limitations over the next two years. Therefore, physical inactivity increased the average number of incident IADL limitations by 0.15 for the most cognitively impaired category (p-value for difference = 0.007). Among people in the low dementia probability category, physical inactivity was associated with an extra 0.14 new IADL limitations at each wave (p-value for difference =0.004). Consistent with the multiplicative models, alcohol use, smoking, and depression had little benefit on an absolute scale for individuals in the highest dementia probability quartile (figures 1b–1d).

DISCUSSION

Results from this large, prospective cohort study suggest that not consuming alcohol, smoking, and depression have limited effects on the incidence of IADL limitations among cognitively impaired individuals. In contrast physical inactivity is associated with an increased risk of incident IADL limitations for both the high and low dementia risk groups. This paper builds on our previous work on these modifiers, cognitive impairment, and ADL limitations by examining the effect of the modifiers on IADL limitations in both cognitively normal and cognitively impaired populations.

A previous meta-analysis concluded that cognitive status influences functional outcomes,[3] but did not explore whether the impact of cognitive status on functional outcomes can be modified by individual level health behaviors. Several of the factors that we examined, including smoking,[6–10] depression,[28] and high levels of alcohol consumption,[29] have already been associated with functional decline or impairment among those with normal cognition. Fewer studies have examined effects of these modifiers among those with cognitive impairment or examined IADLs as a separate outcome from ADL limitations. A recent review of the literature on depression and disability found that of the 12 studies which measured cognition, only 6 reported that baseline or incident depression predicted disability independent of cognition.[28] However, these studies examined ADLs or a composite of ADLs and IADLs as their measure of disability. Since IADLs are typically more cognitively demanding than ADLs, we hypothesized that it was less likely that these individual-level factors would ameliorate the effects of cognitive impairment on IADL limitations.[30]

Intervention studies suggest that physical activity may improve functional outcomes among those with dementia or mild cognitive impairment.[31],[32, 33] Additionally, a previous

observational study examined the effect of physical activity on both ADL and IADLs among community-based elderly participants without dementia. They observed decreased in the risk of incident ADL (HR=0.89; 95% CI: 0.83–0.95) and IADL (HR=0.93; 95% CI: 0.89–0.99) limitations for each additional hour of physical activity.[34] However, this study did not examine whether the impact of physical activity on incident IADL limitations varied by level of baseline cognitive function. Our study expands upon these results by examining whether the impact of physical inactivity on IADL limitations varies by cognitive status. Physical inactivity increased the risk of incident IADL limitations among those with and without cognitive impairments, with evidence that the effect was stronger in relative terms among those without cognitive impairments. In addition to the relative impact of physical inactivity on the risk of IADL limitations, the magnitude of the effect estimate in absolute terms was clinically meaningful, especially given the other known benefits of physical activity on cardiovascular and cognitive health. Although apraxia and cognitive losses may inhibit the ability of the cognitively impaired person to participate in some activities, clinicians and caregivers can work together to develop activities in which the cognitively impaired person can participate.[35]

Although over 3.4 million Americans over the age of 71 are affected by MCI or dementia [36], there is no known cure and treatments have modest if any benefits. Median survival after diagnosis with dementia is 4.1 years for men and 4.6 years for women.[37] Therefore, it is of utmost importance to develop strategies to preserve quality of life and, to the extent possible, independence, for patients as long as possible. Overall, our findings highlight the tremendous challenges in helping cognitively impaired individuals maintain IADL independence. Even with behavioral modifications designed to help preserve independence in basic ADLs, patients with dementia or cognitive impairment are likely to need substantial assistance with IADLs. Unfortunately, many IADLs are not considered part of routine medical care or even home health care. For individuals with cognitive impairment, IADL limitations may lead to earlier institutionalization or major burdens on caregivers. For patients without extensive networks to help with IADLs, such limitations may pose serious threats to health and safety. Providing direct support for IADLs, alongside behavioral interventions to preserve ADL independence and treatment of other comorbidities like depression, should be a key strategy for preserving quality of life for individuals with cognitive impairment or early dementia.

We acknowledge important limitations in our study, including the potential for residual confounding by factors like physical impairments that may affect both our individual-level risk factors and incident IADL limitations. Additionally, this study examines overall number of IADL limitations and does not consider the order in which the limitations occur, the co-occurrence of ADL and IADL limitations, or back-transitions due to resolution of IADL limitations. Additionally, our study only examined the presence or absence of an IADL limitation and did not consider whether individual-level modifiers impact the severity of the IADL limitation. It is possible that these modifiers may reduce the severity of IADL limitations but our measures were not sufficiently sensitive to detect modest improvements. Also, this study only looks at four individual-level modifiers and there may be other individual-level characteristics, behaviors, and health factors for incident IADL limitations (for example, dietary factors[38] [39], social activities[40], body mass index, disease

burden, lower extremity functional limitation, low frequency of social contacts, and vision impairment [4]) which may modify the association between cognitive impairment and incidence IADL limitations. Our use of data from a large, nationally representative cohort study is a major strength of this study. Since the data were collected longitudinally over several years, we assessed cognitive status and individual-level modifiers prior to outcome assessment. Additionally, we used inverse probability weighting to control for the possibility that cognitive functioning may impact future modifier status and selective attrition. Another strength of this study was the use of imputed dementia probability categories. Although those with severe cognitive impairment often cannot complete cognitive assessments and are excluded from analyses, we used proxy reports of cognitive status to determine a subject's dementia probability category. This allowed us to retain those individuals with severe cognitive impairments.

CONCLUSION

We found a strong association between dementia probability and incident IADL limitations. Physical inactivity was associated with an increased risk of incident IADL limitations regardless of cognitive status. However, not consuming alcohol, smoking, and depression did not have major impacts on IADLs among individuals with cognitive impairments. Given the increased cognitive demands of IADLs, it may be difficult to use some of the individual-level factors examined in this study to ameliorate the impact of cognitive impairment on IADL limitations. In addition to supporting continued physical activity among the cognitively impaired, direct support for IADLs may also be an important component of providing health care to individuals with cognitive impairment or dementia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by the Telemedicine and Advanced Technology Research Center (TATRC) at the U.S. Army Medical Research and Materiel Command (USAMRMC) through award W81XWH-12-1-0143. Dr. Capistrant was also supported by generous support from the National Institutes of Health (T32 HD007168 and R24 HD050924). Ms. Marden was also supported by the National Institutes of Health (T32 NS048005).

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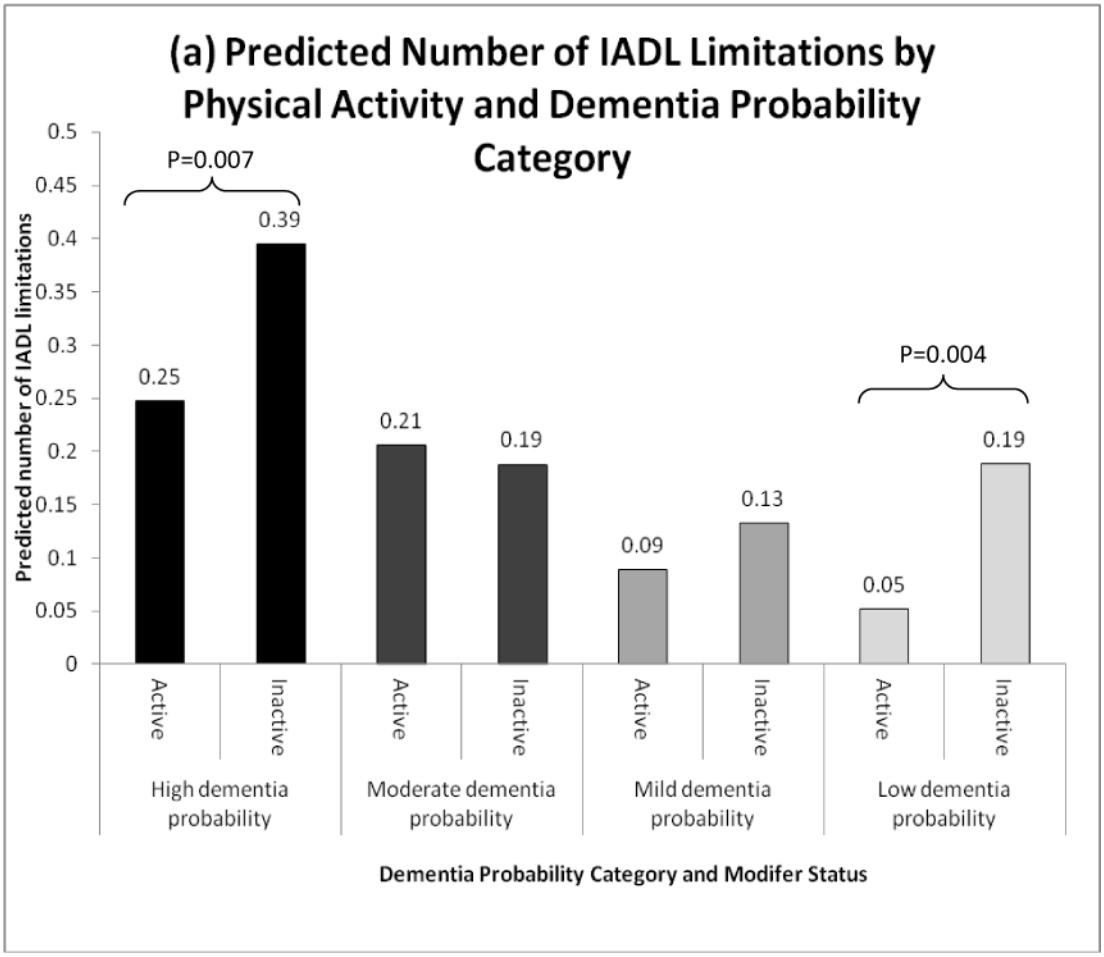

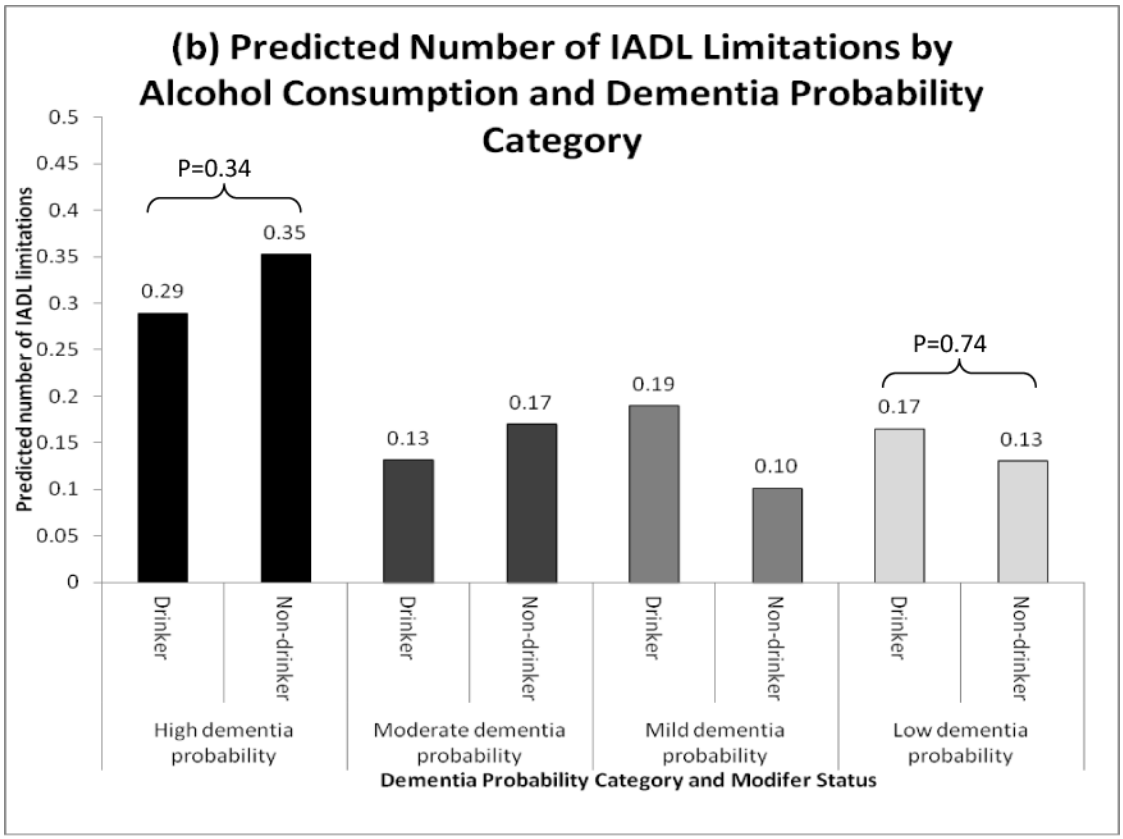

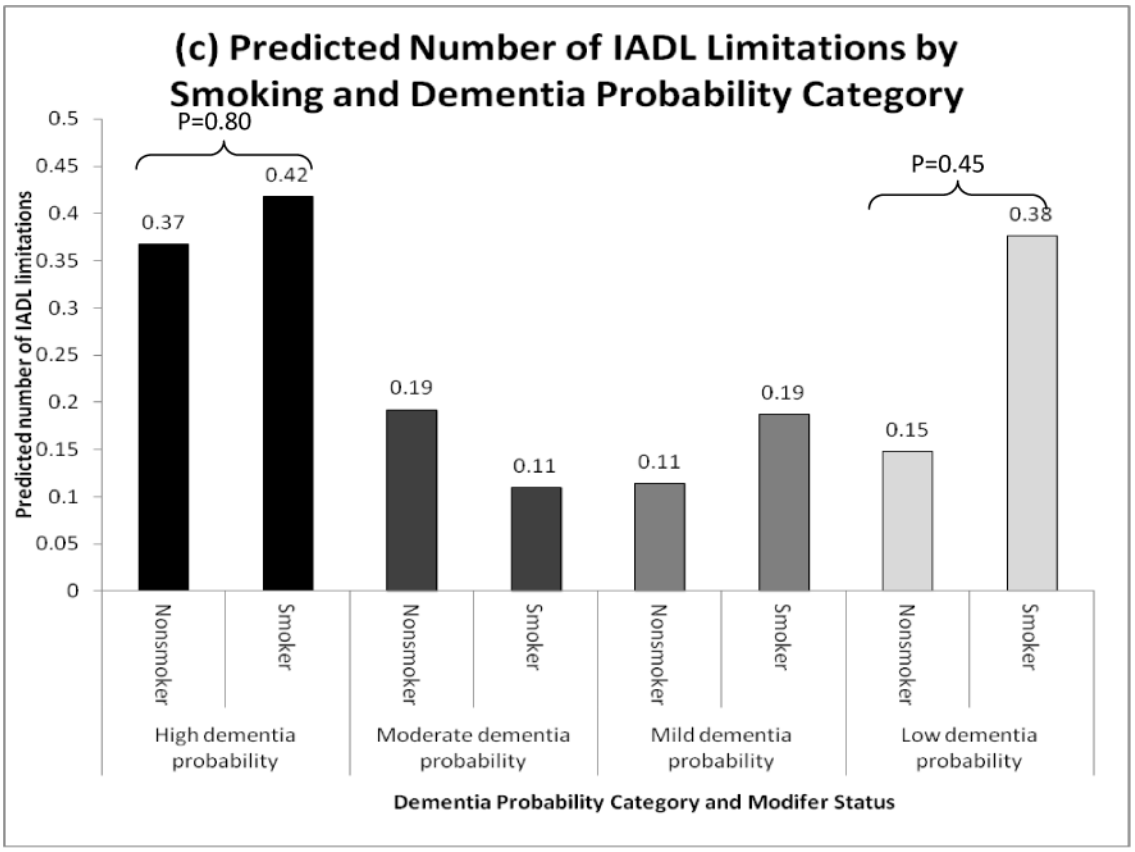

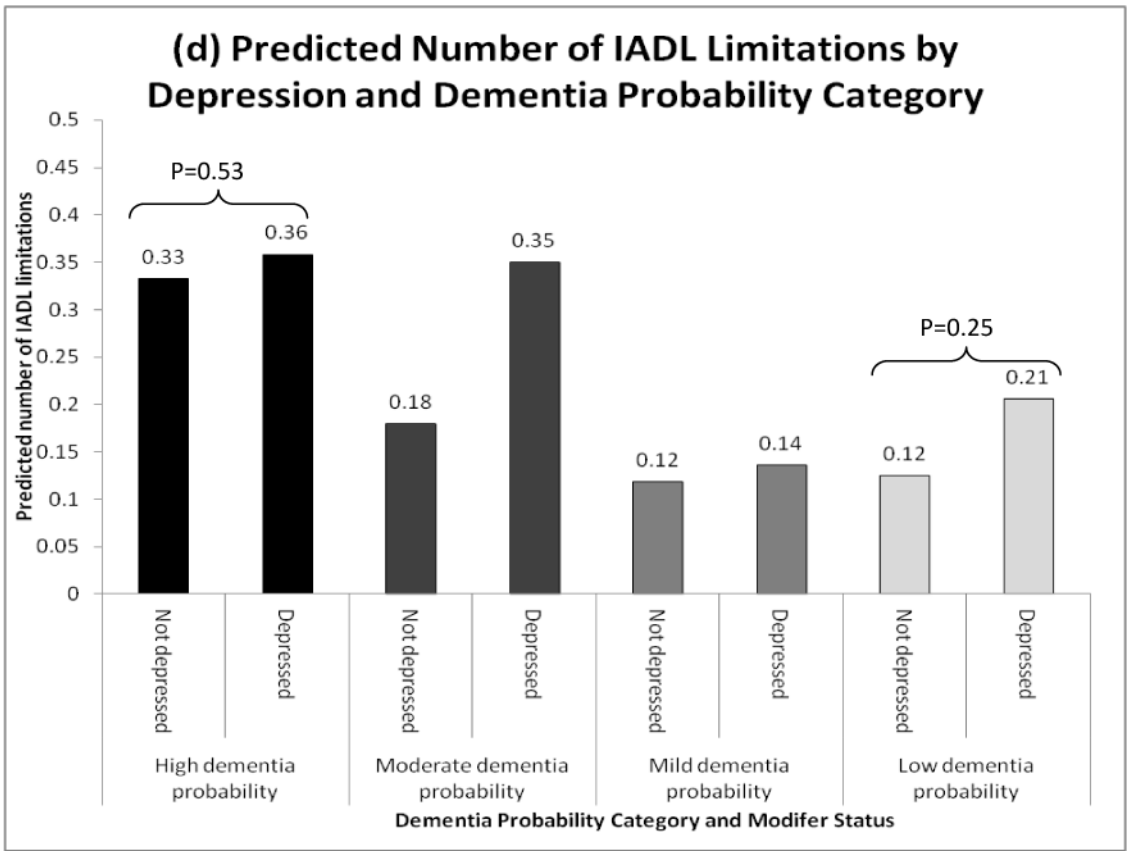

Figure 1.

Predicted number of incident IADL limitation per wave, by modifier and dementia probability category, with statistical significance tests for differences in absolute effects for those in the highest and lowest dementia probability categories.

Legend: IADL limitations were assessed each wave (every two years). We adjusted for the following potential time-constant confounders: age, age squared, sex, race, southern birthplace, education, mother's and father's educations, and height. Additionally, we adjusted for the following time-varying confounders using an inverse probability weighting approach: marital status, log of household size-adjusted wealth, body mass index, a summary score of self-reported comorbidities, and our modifiers.

Table 1

Baseline characteristics of those included in the analysis of dementia probability category and any incident IADL limitation by dementia probability category at baseline.

Characteristic	Dementia Probability Category at Baseline			
	High Dementia Probability (N= 1305)	Moderate Dementia Probability (N= 1304)	Mild Dementia Probability (N= 1305)	Low Dementia Probability (N= 1305)
Age (mean, std)	76.5 (6.4)	72.6 (5.5)	72.0 (5.2)	70.2 (4.6)
Gender (% male)	55.5	56.2	33.4	23.4
Race (% black)	14.8	8.8	8.5	6.3
Southern birthplace (%)	15.9	14.0	12.3	10.7
Years of education (mean, std)	11.2 (3.2)	12.5 (2.7)	12.8 (2.6)	13.4 (2.4)
Mother had ≥8 years of education (%)	43.1	50.8	55.1	58.0
Father had ≥8 years of education (%)	38.2	43.8	45.9	49.6
Marital status				
Married (%)	57.4	68.9	64.5	64.2
Divorced/separated (%)	5.4	5.4	5.8	8.2
Widowed (%)	34.0	21.7	25.9	24.4
Never married (%)	3.1	4.0	3.8	3.1
Physically inactive (%)	63.0	54.5	51.3	48.1
Not drinking (%)	77.7	71.2	70.0	69.4
Current smoking (%)	7.6	8.4	9.7	9.6
Current depression (%)	13.6	11.4	8.8	8.1
Low household-size adjusted income (%)	30.5	18.1	15.3	14.4
Body mass index (mean, std)	26.0 (4.2)	26.5 (4.2)	26.6 (4.8)	26.2 (4.5)
Number of comorbidities (mean, std)	1.7 (1.2)	1.6 (1.2)	1.6 (1.2)	1.4 (1.1)

Table 2

Distribution of dementia probability categories and total number of people reporting incident IADL limitations by year.

Dementia Probability Category	Year					Number of people reporting incident IADL limitations (n)	Mean number of limitations reported among those reporting limitations (n, std)
	2002	2004	2006	2008	2010		
High dementia probability (n)	1305	1094	1002	869	699	1085	2.20 (1.44)
Moderate dementia probability (n)	1304	1114	896	690	572	482	1.64 (1.09)
Mild dementia probability (n)	1305	1081	885	724	529	307	1.49 (0.94)
Low dementia probability (n)	1305	956	623	449	324	179	1.63 (1.16)
Number of people reporting incident IADL Limitations (n)	524	512	400	290	327	2053	
Mean number of limitations reported (n, std)	1.90 (1.29)	1.81 (1.25)	1.88 (1.30)	1.91 (1.26)	2.14 (1.46)		1.91 (1.31)

List of abbreviations: IADL = instrumental activities of daily living; std = standard deviation

Note: The number of people declines from left to right because of censoring due to incident IADL limitations, death, or dropout.

Table 3

Association between dementia probability category and incident IADL limitations including interactions between dementia probability and individual health factors.

	OR	95%	CI	p-value
Physical Activity				
No Physical Activity	1.60	1.16	2.19	<0.01
Low dementia probability	0.21	0.12	0.38	<0.01
Low dementia probability *No Physical activity	2.28	1.05	4.93	0.04
Mild dementia probability	0.36	0.21	0.62	<0.01
Mild dementia probability *No Physical activity	0.94	0.50	1.74	0.83
Moderate dementia probability	0.83	0.54	1.29	0.41
Moderate dementia probability *No Physical activity	0.57	0.34	0.96	0.03
Drinking				
Not Drinking	1.22	0.79	1.88	0.39
Low dementia probability	0.57	0.16	2.01	0.38
Low dementia probability *Not Drinking	0.65	0.17	2.48	0.53
Mild dementia probability	0.66	0.32	1.34	0.25
Mild dementia probability *Not Drinking	0.44	0.21	0.93	0.03
Moderate dementia probability	0.45	0.25	0.82	<0.01
Moderate dementia probability *Not Drinking	1.06	0.57	1.97	0.85
Smoking				
Smoking	1.00	0.36	2.74	0.79
Low dementia probability	0.40	0.24	0.68	<0.01
Low dementia probability *Smoking	2.24	0.33	15.01	0.41
Mild dementia probability	0.31	0.24	0.40	<0.01
Mild dementia probability *Smoking	1.44	0.37	5.61	0.60
Moderate dementia probability	0.52	0.42	0.53	<0.01
Moderate dementia probability *Smoking	0.50	0.11	2.38	0.39
Depression				
Depression	1.08	0.79	1.47	0.63
Low dementia probability	0.37	0.24	0.58	<0.01
Low dementia probability *Depression	1.53	0.70	2.77	0.28
Mild dementia probability	0.36	0.27	0.48	<0.01
Mild dementia probability *Depression	1.06	0.41	2.77	0.90
Moderate dementia probability	0.54	0.41	0.71	<0.01
Moderate dementia probability *Depression	1.81	1.03	3.17	0.04

Note: The reference group for all analyses presented above is the highest dementia probability group. Therefore, the OR for each modifier (e.g., no physical activity, smoking) provides the estimated effect of that modifier among individuals in the highest dementia probability group. The asterisks indicate coefficients for the interaction term between the dementia probability group and the modifier.

Archives of Gerontology and Geriatrics 65 (2016) 140–145

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Modifiable risk factors for nursing home admission among individuals with high and low dementia risk

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ARTICLE INFO

Article history:
Received 15 October 2015
Received in revised form 29 February 2016
Accepted 18 March 2016
Available online 19 March 2016

Keywords:
Nursing home
Risk factors
Cognitive function
Epidemiology

ABSTRACT

Background: Strategies to prevent or delay nursing home admission in individuals with cognitive impairment are urgently needed. We hypothesized that physical inactivity, not consuming alcohol (as opposed to moderate alcohol use), and having a history of smoking predict nursing home admission among individuals with normal cognitive function, but these behavioral factors would have attenuated associations with nursing home admission among individuals with impaired cognition.

Methods: We performed a prospective cohort study among 7631 Health and Retirement Study participants aged 65+ at baseline. Baseline dementia risk (high versus low, based on brief psychometric assessments and proxy reports) and modifiable risk factors (physical inactivity, ever smoking, and not consuming alcohol) were used to predict nursing home admission in pooled logistic regression models. We evaluated whether estimated effects of modifiable factors varied by dementia risk, comparing both relative and absolute effects using interaction terms between dementia risk and each modifiable risk factor.

Results: Low dementia probability was associated with lower nursing home admission risk (RR = 0.49; 95% CI: 0.41, 0.59). Physical inactivity (RR = 1.27; 95% CI: 1.15, 1.41), ever smoking (RR = 1.12; 95% CI: 1.01, 1.25), and not consuming alcohol (RR = 1.28; 95% CI: 1.13, 1.45) predicted increased relative risk of nursing home admission regardless of cognitive status. The relative effects of modifiable risk factors were similar for those with low and high dementia risk.

Conclusion: Although cognitive impairment associated with incipient dementia strongly predicts nursing home admission, this risk can be partially ameliorated with modifiable risk factors such as physical activity.

1. Introduction

Spending on nursing home care in the United Stated is projected to exceed $167 billion in 2015 (Keehan et al., 2015). In addition to its high cost, placement in a nursing home has been associated with many adverse outcomes including questionable quality of care for the patient and emotional distress for the caregiver (Institute of Medicine (U.S.). Committee on Improving Quality in Long-Term Care, Wunderlich, & Kohler, 2001; Kane, 2001; Schulz et al., 2004). The vast majority of elderly individuals would prefer to remain in their homes as they age (National Council on Aging, 2012). The combination of high costs, negative health outcomes, and consideration of preferences to "age in place" has resulted in efforts to identify factors associated with nursing home placement with the hope of developing interventions to delay nursing home placement. Cognitive impairment strongly predicts risk of nursing home admission (Gaugler, Duval, Anderson, & Kane, 2007; Luppa et al., 2010), more than doubling the risk of nursing home admission according to a large *meta*-analysis (Gaugler et al., 2007). Given the strong association between cognitive function and risk of nursing home admission, there is a growing interest in finding factors which may delay nursing home placement even among those with cognitive impairment.

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http://dx.doi.org/10.1016/j.archger.2016.03.016
0167-4943/

Prior research among dementia patients has focused mostly on demographics, co-morbidities, depressive symptoms, presence of functional limitations, and caregiver characteristics as potential predictors of nursing home placement (Luppa, Luck, Brahler, Konig, & Riedel-Heller, 2008). Evidence for other modifiable behaviors, such as alcohol consumption, smoking, or physical activity is limited. Studies in the general population suggest that smoking status and alcohol consumption influence the risk of nursing home admission (Deng et al., 2006; Kaplan et al., 2014; McCallum, Simons, Simons, & Friedlander, 2007; Valiyeva, Russell, Miller, & Safford, 2006; Wang, Mitchell, Smith, Cumming, & Leeder, 2001; Warner, McCammon, Fries, & Langa, 2013). For example, although high levels of alcohol consumption is harmful to health (Stahre, Roeber, Kanny, Brewer, & Zhang, 2014), some studies have observed that moderate alcohol consumption is associated with a reduction in the risk of nursing home placement (Kaplan et al., 2014; McCallum et al., 2007). One study showed that this association persisted even after adjusting for socioeconomic factors (Kaplan et al., 2014). Physical function affects nursing home admission independent of cognitive function (Luppa et al., 2010), so smoking status and alcohol consumption may also impact the risk of nursing home admission among those with cognitive impairment through their impacts on physical functioning. Evidence for the effect of physical activity on the risk of nursing home placement in either the cognitively normal or the cognitively impaired is much more limited. Although low physical activity levels predict functional limitations in the general population (Stuck et al., 1999) and among those with cognitive impairment (Blankevoort et al., 2010) and functional limitations are strongly associated with the risk of nursing home placement in both the general population and among those with dementia (Gaugler et al., 2007; Gaugler, Yu, Krichbaum, & Wyman, 2009), evidence for the effect of physical activity on nursing home admission risk in the general population is mixed. Studies among those with cognitive impairment or dementia have often focused on the effect of exercise training on fitness, physical function, cognitive function and positive behavior (Heyn, Abreu, & Ottenbacher, 2004), but have not assessed the effect of physical activity on the risk of institutionalization.

Although there are no effective treatments to cure dementia, physical activity, smoking, and alcohol consumption can all be modified, and accurate information about the likely impact of such behaviors on nursing home risk is important for patients, caregivers, and clinicians. These modifiable risk factors may provide opportunities to reduce the risk of institutionalization even among those with cognitive impairment. On the other hand, cognitive impairment may so dramatically increase nursing home admission that none of the modifiable factors are relevant. In other words, among individuals with cognitive impairment, no other factors may offset or exacerbate risk. Distinguishing these possibilities will help design and target effective interventions to reduce or delay nursing home admissions.

Using data from the Health and Retirement Study (HRS), we examined the effect of cognitive status and modifiable risk factors on the risk of nursing home admissions. We also evaluated interactions between cognitive status and each risk factor to determine if the relative or absolute impact of each modifiable factor differs based on the individual's cognitive status. We hypothesized that physical inactivity, not consuming alcohol, and ever smoking would predict an increase in risk of nursing home admission among individuals with normal cognitive function, but effects of these risk factors would be attenuated in both relative and absolute terms among individuals with impaired cognition.

2. Methods

Briefly, the HRS is a nationally representative cohort of Americans aged 50 years or older and their spouses (Heeringa, 1995; Juster & Suzman, 1995). These analyses were restricted to those participants who were aged 65 years or older in 2000 because cognitive assessments were performed biennially only for those aged 65 years or older.

HRS was approved by the University of Michigan Health Sciences Human Subjects Committee.

2.1. Outcomes assessment

Our primary outcome was a binary indicator of first self-reported nursing home admission defined as a facility which provides all of the following services for its residents: dispensing of medications, 24-h nursing assistance and supervision, personal assistance, room and meals. In the case of decedents or other participants who are not able to respond, information on nursing home admission was provided by proxy informants (typically a spouse or other close family member). For respondents who were alive at the time of the interview, using data from RAND (St. Clair et al., 2010), we determined whether the participant or their proxy reported any nursing home stay since the previous interview wave (i.e. in the past two years) or if the respondent or their proxy reported currently living in a nursing home or other health care facility at the time of the interview. For respondents who were not alive at the time of the interview, we used information from the HRS Exit interviews with proxy respondents to determine if the respondent was living in a nursing home at the time of his or her death. Individuals who reported nursing home stays or currently living in a nursing home in 1998 or 2000 were excluded from all analyses. We assessed outcomes through the 2012 interview wave.

2.2. Cognitive assessment

Our measure of cognitive impairment was imputed dementia probability score which has been described in detail previously (Wu et al., 2013). Briefly, direct and proxy-assessed cognition were calibrated against dementia diagnoses according to DSM-III-R and DSM-IV criteria in a sub-sample of HRS participants (C statistic = 94.3%). The theoretical range of the imputed score was from 0 (no chance this person has dementia) to 1 (individual certain to have dementia) with an actual range of 0.51×10^{-13} to 0.99 for the individuals included in these analyses. We divided dementia probability score at each wave into two categories (high and low dementia probability) based on the 90th percentile of the dementia probability in 2000 (90th percentile of dementia probability = 0.197). Those below the cutpoint were used as the reference group for all analyses (they represent "normal" cognitive function). Imputed dementia probabilities were not available for Hispanics so they were excluded from these analyses.

2.3. Risk factors for nursing home admission

The risk factors considered in this analysis were physical inactivity, not consuming alcohol, and ever smoking. We slightly modified the RAND version (St. Clair et al., 2010) of these variables to create dichotomous variables consistent with our previous work (Nandi, Glymour, & Subramanian, 2014; Rist, Capistrant, Wu, Marden, & Glymour, 2014). We dichotomized physical activity as active (vigorous activity 3 or more times per week) versus inactive (vigorous activity less than 3 times per week). We classified alcohol consumption as heavy drinking ($\geq$2 drinks/day), moderate drinking (more than zero and fewer than two drinks per day), and not drinking (reference). To calculate drinks per day, the number of drinks consumed on days the participant drinks was multiplied by the number of days per week the participant reported drinking and the result was divided by seven. Ever smoking status was a binary variable (yes/no). We used values of

the exposure variables as reported in 2000, or, when values for the 2000 wave were missing (n = 15), in 1998.

2.4. Covariates

In addition to including dichotomized dementia probability, physical activity, alcohol consumption, and smoking status, all analyses were adjusted for demographics, socioeconomic status, and comorbidities. All of these potential confounders were assessed in 1998 prior to assessment of dementia probability and our risk factors and included: age (centered, continuous), centered age squared (continuous), gender, race (black versus other), southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for General Education Development (GED) completion), mother's and father's education ($\leq$8 years, >8 years), height (gender-specific baseline quartiles), log of household size-adjusted wealth (continuous), body mass index ($<25\,kg/m^2$ (reference), 25 to $<30\,kg/m^2$, $\geq 30\,kg/m^2$), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), marital status (married, widowed, divorced or never married), depressive symptoms (<3 versus ≥ 3 depressive symptoms in the past two weeks using a modified 8-item Centers for Epidemiologic Studies-Depression scale), any limitation (yes/no) in five ADLs (getting across a room, dressing, bathing, eating, and getting in and out of bed), any limitation (yes/no) in five IADLs (using a phone, managing money, taking medication, shopping for groceries, and preparing hot meals) and interview wave. Participants missing any covariate in 1998 (N = 804) were excluded from all analyses.

2.5. Statistical analysis

We used pooled logistic regression models to calculate odds ratios (ORs), which, with rare outcomes, approximate hazard ratios in continuous time survival analysis. Participants were censored at last interview, death, or first admission to a nursing home.

First we explored the association between our risk factors and nursing home admission and included dichotomous dementia probability category (high versus low) as a covariate in these models. We also included the demographic, socioeconomic, and comorbidity variables listed above. Next, we used two different approaches to determine if cognitive impairment modified the association between the risk factors and nursing home admission risk. In the first approach, we included an interaction term between dementia probability category and each risk factor (in separate models for physical activity, alcohol consumption, and smoking) to determine if the risk factor had a different relative effect on nursing home admission risk depending upon the participant's dementia category. The models also included the dichotomous dementia probability category, the remaining risk factors (without interaction terms between those risk factors and dementia category), and the demographic, socioeconomic, and comorbidity variables listed earlier. In the second approach, we calculated the marginal probability of nursing home admission according to risk factor status and dementia category. This allowed us to compare the absolute effects of both the "beneficial" and "adverse" value of each risk factor on nursing home admission probability by dementia category.

3. Results

In 2000, HRS included 9524 individuals aged 65 or older who were not Hispanic. We excluded the 569 participants who reported a nursing home stay or living in a nursing home in 1998 or 2000 or who did not answer the questions on nursing home stays or residence in 1998 or 2000. We also excluded the 405 participants without information on nursing home admission in the 2002 wave and the 115 people missing information on dementia probability in 2000. Finally, we excluded the 804 people missing information on any of our covariates or modifiers, leaving 7631 participants for our analyses.

Respondents with high dementia probability had a higher prevalence of physical inactivity, not consuming alcohol, and ever smoking than those with low dementia probability (Table 1). During follow-up, 2353 people reported admission to a nursing home (cumulative incidence = 30.8%).

Table 2 shows the association between our risk factors and low dementia probability and risk of nursing home admission. Those with low dementia probability had roughly half the risk of nursing home admission during each two-year interview interval (RR = 0.49; 95% CI: 0.41, 0.59) compared to those with high dementia probability. Physical inactivity compared to being active (RR = 1.27; 95% CI: 1.15, 1.41), ever smoking compared to never smoking (RR = 1.12; 95% CI: 1.01, 1.25), and not consuming alcohol (RR = 1.28; 95%

Table 1
Characteristics of those included in the analysis of dementia probability category, modifiable risk factor status, and risk of nursing home admission by dementia probability category at baseline.

Characteristic	High Dementia Probability (N = 763)	Low Dementia Probability (N = 6868)
Age (mean, std)	80.3 (7.1)	71.5 (6.2)
Gender (% male)	35.3	42.5
Race (% black)	20.8	10.9
Southern birthplace (%)	21.4	14.1
Years of education (mean, std)	10.0 (3.8)	12.4 (2.8)
Mother had $\geq$8 years of education (%)	38.3	51.2
Father had $\geq$8 years of education (%)	35.7	43.6
Physically inactive (%)	80.9	56.1
Non-drinker (%)	88.5	72.6
Heavy drinker (%)	2.4	5.3
Ever smoker (%)	50.9	58.3
Depressed (%)	23.1	12.1
Body mass index (mean, std)	25.3 (4.7)	26.5 (4.7)
Number of comorbidities (mean, std)	2.0 (1.3)	1.7 (1.3)
Marital status*		
Married	42.6	65.7
Divorced	5.5	7.3
Widowed	49.2	24.6
Never married	2.8	2.5

Table 2
Odds ratios for prediction of nursing home admission as a function of dementia risk, physical inactivity, alcohol use, and ever smoking.

	Nursing Home Admission		
	OR	95%	CI
Low Dementia Probability	0.49	0.41	0.59
Low Physical Activity	1.27	1.15	1.41
No Alcohol Consumption	1.28	1.13	1.45
Heavy Alcohol Consumption	1.44	1.13	1.82
Ever Smoking	1.12	1.01	1.25

Note: Model is simultaneously adjusted for all of the risk factors.

CI: 1.13, 1.45) or heavy alcohol consumption (RR = 1.44; 95% CI: 1.13, 1.82) compared to moderate alcohol consumption predicted increased risk of nursing home admission.

We next examined whether these factors had different effects among individuals at risk of dementia than among cognitively normal elders. There was no statistically significant interaction between dementia probability and physical inactivity ($p = 0.92$), smoking ($p = 0.40$), no alcohol consumption ($p = 0.28$) or heavy alcohol consumption ($p = 0.69$), indicating that the relative harm of the modifier was similar for those with low and high dementia probability (Table 3).

Because similar relative effects may conceal differences in absolute effects, we also estimated the marginal probability of nursing home admission for each risk factor among those with high and low dementia probability (Fig. 1). Physical activity was associated with an decreased absolute probability of nursing home admission for those with low dementia probability. However, the magnitude of the estimated effect of physical activity on the probability of nursing home admission was slightly higher among those with high dementia probability (2.39% point difference) than among those with low dementia probability (1.55% point difference). Never smoking was not associated with significantly lower probability of nursing home admission among those with high dementia probability; the estimated absolute effect among the high dementia probability group (2.55% point difference) was larger than among the low dementia probability (0.07% point difference) group but this difference was not statistically significant. Moderate drinking compared to not consuming alcohol predicted lower risk of nursing home admission among those with low dementia probability (1.40% point difference) and among those with high dementia probability (4.84% point difference). Moderate drinking compared to heavy drinking predicted lower risk of nursing home admission among those with low dementia probability (2.48% point difference) but not among those with high dementia probability (1.33% point difference).

Table 3
Association between dementia probability category and nursing home admission including interactions between dementia probability and each risk factor.

	Nursing Home Admission		
	OR	95%	CI
Physical Activity			
Low Dementia Probability	0.48	0.35	0.67
Low Dementia Probability × Low Physical Activity	1.02	0.70	1.47
Low Physical Activity	1.25	0.88	1.78
Alcohol Consumption			
Low Dementia Probability	0.61	0.38	0.98
Low Dementia Probability × No Alcohol Consumption	0.76	0.46	1.25
No Alcohol Consumption	1.65	1.02	2.66
Low Dementia Probability × Heavy Alcohol Consumption	1.25	0.42	3.72
Heavy Alcohol Consumption	1.17	0.40	3.38
Smoking			
Low Dementia Probability	0.52	0.41	0.67
Low Dementia Probability × Ever Smoking	0.87	0.63	1.20
Ever Smoking	1.27	0.94	1.72

Note: Models all include all of the other risk factors, but do not include interaction terms between the other risk factors and dementia probability. Interaction terms test the null that the relative effect of the risk factor is the same for individuals with high and low dementia probability.

4. Discussion

Results from this study suggest that physical activity, moderate alcohol consumption, and never smoking may protect against nursing home admission risk among older adults overall regardless of cognitive status. The benefits of physical activity, moderate alcohol consumption or never smoking also appear similar for individuals at high risk of dementia compared to cognitively normal individuals. Indeed the point estimates suggest larger absolute effects among those with high risk of dementia. In these data, physically active individuals at high risk of dementia had over a two percentage point lower risk of nursing home admission compared to their sedentary counterparts. Similarly, individuals at high risk of dementia who never smoked had over a two percentage point lower risk of nursing home admission compared to individuals who ever smoked; individuals at high risk of dementia who consume alcohol moderately had over a four percentage point lower risk of nursing home admission compared to those at high risk of dementia who did not consume alcohol.

Few studies have directly considered the interaction between cognitive status and individual level factors like physical activity, smoking, and alcohol consumption. Smith et al. found four factors which were associated with nursing home placement among those with dementia, only one of which was associated with nursing home placement among those without dementia. However, they did not provide a formal statistical comparison of the risk factors among those with and without dementia nor did they consider the three modifiable risk factors we examined in this study (Smith, O'Brien, Ivnik, Kokmen, & Tangalos, 2001).

Most of the research on physical activity and the risk of nursing home admission has been conducted in general population samples, without considering whether the impact of physical activity on nursing home admission varies by cognitive status. A recent *meta*-analysis found "moderate evidence" that physical activity protected against nursing home placement in the general population (Luppa et al., 2010) while another review stated that poor health behaviors (including inadequate nutrition and exercise, smoking, and alcohol consumption) were not associated with institutionalization (Miller & Weissert, 2000). A more recent study further explored the association between physical activity and nursing home admission by stratifying their analyses by age. They reported that physical inactivity was associated with an increased risk of nursing home admissions among those aged 45–64 years at baseline, but not among those aged 65–74 at baseline (Valiyeva et al., 2006).

In our study, we found a significant association of physical activity with nursing home admissions for individuals aged 65 or older at baseline. Given that our previous research in HRS (Rist et al., 2014; Rist, Marden, Capistrant, Wu, & Glymour, 2015) has shown protective effects of physical activity on functional limitations for individuals with and without cognitive impairments, we hypothesize that physical activity may decrease the risk of nursing home placement by decreasing the risk of functional limitations. Functional limitations have been associated with an increased risk of nursing home placement in both those with and without dementia (Gaugler et al., 2007, 2009).

Previous studies have shown an association between current smoking and increased risk of nursing home admission (Valiyeva et al., 2006; Wang et al., 2001). A previous study in HRS observed

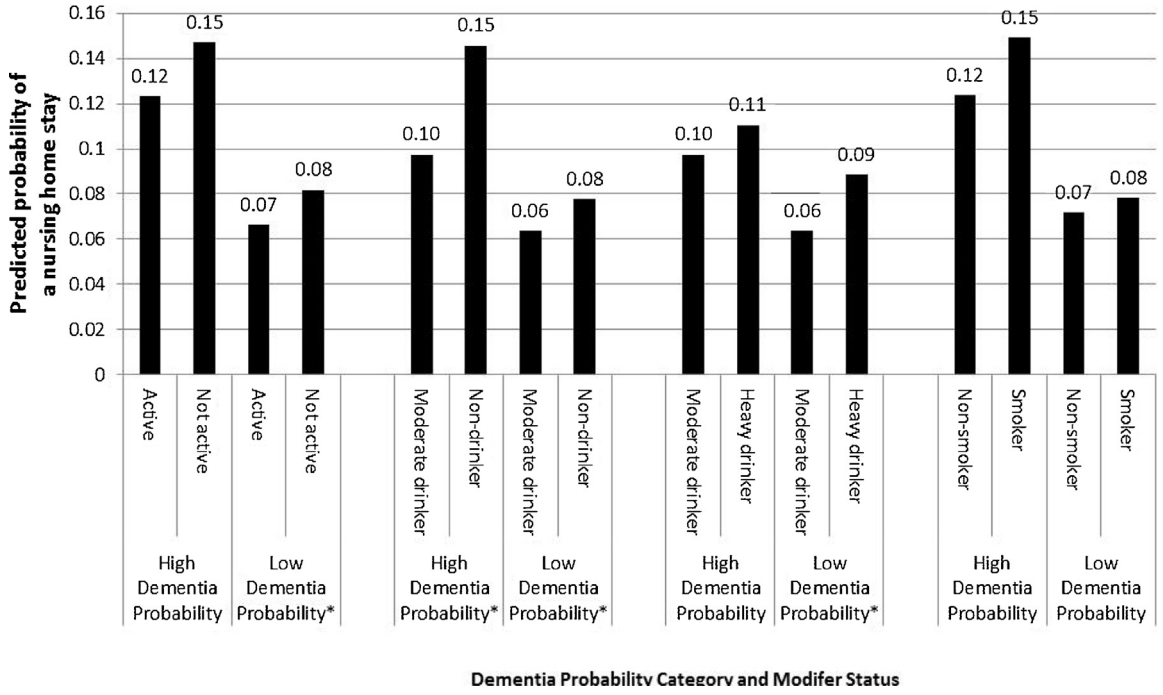

Fig. 1. Predicted probability per wave of nursing home admission by modifier and dementia status. Asterisks indicate a statistically significant difference in the predicted probability per wave of a nursing home admission for those with and without the modifier.

the highest risk of nursing home admission among recent quitters compared to never smokers; individuals who had recently stopped smoking within the past three years had higher risk of nursing home admission than those who had stopped smoking 3 or more years ago or those who remained current smokers (Warner et al., 2013). This suggests that those who quit smoking may do so in part because they are already sick (i.e. reverse causation) and highlights the difficulty with determining the true effect of smoking status on nursing home admission. We categorized smoking as ever smoking versus never smoking because most smokers initiate in late adolescence or early adulthood, making it unlikely that ever/never smoking status is confounded by adult illnesses. With this classification, we found an association between smoking and nursing home admission which did not vary by dementia probability status.

Our findings are consistent with some prior studies reporting a protective effect of moderate alcohol consumption on the risk of nursing home placement (Kaplan et al., 2014; McCallum et al., 2007). This finding is important for considerations of whether older adults who are currently moderate drinkers should be encouraged to cease alcohol use. Our evidence shows no indication that alcohol cessation would be of benefit but rather suggests non-drinkers are at higher risk of nursing home admission than moderate drinkers. However, our study did not consider lifetime history of alcohol consumption and we do not know if the non-drinkers in our sample previously had alcohol problems or stopped for health reasons. Further, very few study participants were heavy drinkers, so our findings provide little insight into correlates of heavy alcohol use. While some elderly may need to reduce their alcohol consumption due to health issues or medication interactions, the evidence on moderate alcohol use and reduced risk of nursing home admissions should be considered when advising healthy older adults who consume alcohol in moderation and their families about behavioral change.

Our study is observational, and more rigorous designs will be needed to provide conclusive evidence of causality. Given the potential public health impact of delaying nursing home admission, especially in cognitively impaired adults, this research is a priority. An important limitation of our study is the potential for misreporting nursing home stays. To address this, we used both self and proxy reports, but there remains the possibility that some events were missed. We also used baseline values of all predictor variables, which likely attenuated associations. We chose this approach to reduce the impact of confounders such as incipient, undiagnosed illness, but such factors may nonetheless be relevant. We did not have information on lifetime history of behaviors and could not examine whether behavioral changes predicted nursing home admission. We only examined first nursing home admission and did not consider the effect of our factors on multiple admissions or on length of stay in a nursing home; these are important outcomes for future research. Also, we only considered three modifiable risk factors. It is well recognized that nursing home admission is a complex process involving interactions between predisposing factors, such as demographic factors, social characteristics, and health factors; enabling factors, such as personal, familial, and community enabling resources; and need factors, such as the most immediate cause of health service use and both perceived and evaluated health status (Andersen, 1968). Future research will be needed to determine how these individual level factors and cognitive status may interact with other factors, particularly family-level factors and caregiver characteristics.

Our study has several strengths including the use of data from a large, nationally representative cohort study. We considered both relative and absolute effects, noting that because nursing home admission is much more common among individuals at high risk of dementia, a small relative increase in risk of admission may have a large absolute impact. For this reason, absolute measures are often more relevant for public health impact evaluation (Poole, 2010).

In conclusion, we have shown that physical inactivity, ever smoking, and not consuming alcohol predict risk of nursing home admission; the relative effects of these modifiable risk factors appeared similar in those with low and high dementia probability. This highlights the need to include institutionalization as a potential outcome when evaluating the effectiveness of physical

activity interventions because reductions in nursing home admissions may substantially improve the cost-benefit profile of an intervention. When examining the influence of smoking status on the risk of institutionalization, ideally we want to examine whether quitting smoking decreases the risk of institutionalization. However, in this observational data, we were unable to answer that question due to concerns about individuals quitting smoking because of poor health. Future research using a different study design is needed to examine whether quitting smoking may decrease the risk of institutionalization independent of underlying health status. Finally, alcohol consumption is often regulated or discouraged for older adults, even those who have a long-term history of moderate drinking. For example, nearly 37% of nursing homes examined in a recent study do not allow alcohol consumption for any residents (Klein & Jess, 2002). However, it is important for patients, caregivers, and clinicians to have accurate information about the potential benefits of moderate alcohol consumption.

Acknowledgements

Study Funding: This work was supported by the Telemedicine and Advanced Technology Research Center (TATRC) at the U.S. Army Medical Research and Materiel Command (USAMRMC) through award W81XWH-12-1-0143.

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JECH Online First, published on May 25, 2016 as 10.1136/jech-2016-207241

Are self-reported neighbourhood characteristics associated with onset of functional limitations in older adults with or without memory impairment?

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▸ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/jech-2016-207241).

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Received 20 January 2016
Revised 15 April 2016
Accepted 18 April 2016

To cite: Nguyen TT, Rist PM, Glymour MM. *J Epidemiol Community Health* Published Online First: [*please include* Day Month Year] doi:10.1136/jech-2016-207241

ABSTRACT

Background Neighbourhood resources may preserve functional independence in older adults, but little is known about whether benefits differ for individuals with normal and impaired memory. We evaluated the extent to which neighbourhood context was related to onset of instrumental and basic activities of daily living (I/ADL) limitations and whether relationships were modified by memory impairment.

Methods Health and Retirement Study participants 50+ years of age without baseline I/ADL limitations (n=8726 for IADL and n=8345 for ADL models) were interviewed biennially for up to 8 years. Self-reported neighbourhood characteristics were scaled from 0 (worst) to 1 (best). Memory, assessed by direct and proxy cognitive assessments, was dichotomised at the 20th centile. We used pooled logistic regression models, adjusted for demographics and individual characteristics.

Results Low neighbourhood physical disorder (OR=0.51 (95% CI: 0.37 to 0.69)), high social cohesion (OR=0.46 (0.34 to 0.62)), and high safety (OR=0.59 (0.46 to 0.76)) were associated with reduced incidence of IADL limitations. These neighbourhood characteristics were also associated with lower incidence of ADL limitations (disorder OR=0.59 (0.43 to 0.81)); social cohesion OR=0.60 (0.45 to 0.81)); safety OR=0.74 (0.58 to 0.93)). High social ties were not related to ADLs (OR=1.01(0.80 to 1.28)) or IADLs (OR=0.93(0.74 to 1.17)). The benefits of these neighbourhood characteristics for ADLs were similar among those with and without memory impairment but primarily observed among those without memory impairment for IADLs.

Conclusions Older adults living in neighbourhoods with low physical disorder, high social cohesion and high safety experience lower incidence of IADL and ADL limitations. Memory status modified the estimated effects of neighbourhood characteristics on IADL but not ADL limitations.

INTRODUCTION

Functional disabilities, such as limitations in activities of daily living (ADLs) limitations or instrumental activities of daily living (IADLs), are key determinants of quality of life and institutionalisation in older adults.[1] Disability-associated expenditures are estimated to be $400 billion annually.[2] One of the features of moderate dementia is memory loss sufficient to be a serious handicap to independent living.[3] Costs of healthcare for dementia patients outweigh costs of care for patients with heart disease, cancer, or other conditions in the last five years of life,[4] highlighting the importance of identifying opportunities to delay disability in individuals at risk of dementia.

Contemporary understanding of disability focuses on the gap between physical capacity and contextual demands, a gap that may be directly exacerbated or bridged by neighbourhood factors. Research on the influence of neighbourhood level factors on disability has focused on objective measures of neighbourhood quality,[5 6] such as housing density and land-use diversity.[7] Perceived neighbourhood characteristics may play an important role in shaping activities or behaviours that influence disability. For example, performing IADLs (shopping for groceries, preparing hot meals, managing money, taking medications) may require accessing resources in one's community. Concerns about safety or perceived high neighbourhood physical disorder can inhibit performing these IADLs, regardless of the objective characteristics of the neighbourhood.

The potential impact on neighbourhood context is even more important for individuals with prodromal dementia or subtle cognitive impairments. Individuals may live for years or decades with mild to severe memory impairment,[8] and they are at high risk of incident functional disability. Thus, it is imperative to identify resources that help individuals with memory impairment maintain independence for as long as possible. Previous work on neighbourhood resources that promote functional independence have not evaluated whether these resources also benefit older adults with memory impairment. With increasing age and declining health, people are likely to spend greater amounts of time within their neighbourhood of residence.[9 10] The home and neighbourhood become the main environmental contexts for older adults, superseding other settings such as the workplace. In addition, few studies have examined neighbourhood characteristics and functional limitations in a national sample. It is important to evaluate whether associations between neighbourhood resources and disability can be replicated in a national sample reflecting the diversity of US older adults.

In this paper, we aimed to evaluate the influence of perceived neighbourhood disorder, neighbourhood safety, social cohesion and social ties on incident functional limitations in older adults and assess whether the impact of these neighbourhood level factors differ for people with memory impairment. We hypothesised that low physical disorder, high safety, social cohesion and social ties would be inversely associated with functional limitations but that the benefits would be greater for those without memory impairment.

METHODS

Sample

The Health and Retirement Study (HRS) is a nationally representative longitudinal study of US adults aged 50 and over and their spouses. We restricted our analyses to participants with available information on neighbourhood level variables, memory function, covariates, and IADL and ADL limitations. HRS was approved by the University of Michigan Health Sciences Human Subjects Committee. These analyses were determined to be exempt by the University of California, San Francisco Institutional Review Board.

Beginning in 2006, questions assessing neighbourhood physical disorder and social cohesion were posited in each biennial wave to a rotating, random sample of 50% of the core participants selected as part of enhanced face to face interviews. This study uses 2006 and 2008 neighbourhood data. Neighbourhood variables assessing safety and social ties were asked of all the core participants in every biennial wave, but to be consistent with the timing of the neighbourhood measures above, we used data on safety and social ties from the same wave in which physical disorder and social cohesion were assessed. For participants with neighbourhood data in 2006, outcome data from 2008, 2010 and 2012 were used for follow-up. For participants with data in 2008, we used outcome data from 2010 and 2012.

Self-reported neighbourhood characteristics

We investigated four community-level factors: neighbourhood physical disorder, neighbourhood social cohesion, neighbourhood safety, and neighbourhood social ties. Participants were asked to assess neighbourhood physical disorder by the presence of vandalism/graffiti, vacant or deserted houses, cleanliness of the area, and whether respondents would be afraid walking home at night. The social cohesion scale measured feelings of trust, feeling part of the area, and whether respondents think people are friendly or would help them if they were in trouble. All four items in the physical disorder and social cohesion scales used a seven-point Likert scale. Summary scores were created by taking the average of the items, resulting in scores with a theoretical range from 1 to 7 with higher scores representing higher social cohesion or greater physical disorder.[11] Physical disorder scores were reverse coded by subtracting 8 from the original scores so that higher scores represent lower physical disorder. Scores were set to missing if more than two items were missing. The physical disorder and social cohesion scales were then linearly transformed to match the 0–1 range of the other neighbourhood variables (see below) by subtracting 1 from the original scores and dividing by 6. The physical disorder and social cohesion scales have good internal consistency reliability with Cronbach's αs of 0.81 for physical disorder and 0.85 for social cohesion. To assess neighbourhood safety, respondents were asked how they would rate the safety of their neighbourhood with response options being excellent, very good, good, fair or poor. We dichotomised the neighbourhood safety variable (fair/poor vs good/very good/excellent) based on similar previous research in HRS.[10] To assess social ties to neighbours, participants were asked if they had friends or relatives in the neighbourhood (yes/no) and how often they get together with neighbours for a social visit (dichotomised as 1+ time per month). Following previous research by Osypuk, Ehnholt, Moon *et al* (personal communication, 2015), items were averaged to create an index with a theoretical range of 0–1. Scores were set to missing if values for more than one item were missing. We created a composite measure defined as the mean of the four individual neighbourhood measures.

Table 1 Demographic characteristics of participants

Characteristic	ADL analyses (n=8801)	IADL analyses (n=9156)
Age (mean, SD)	65.7 (9.8)	65.7 (9.7)
Male (%)	40.7	40.5
Black (%)	11.5	11.8
Southern birthplace (%)	14.6	14.9
Years of education (mean, SD)	13.2 (2.6)	13.2 (2.5)
Mother had ≥8 years of education (%)	62.7	62.3
Father had ≥8 years of education (%)	53.0	52.6
Marital status, (%)		
Married	72.5	72.0
Divorced/separated	9.6	9.9
Widowed	15.2	15.5
Never married	2.7	2.6
Currently employed (%)	45.1	44.8
Log household size-adjusted wealth (mean, SD)	11.6 (2.7)	11.6 (2.7)
Log household size-adjusted income (mean, SD)	10.4 (1.1)	10.4 (1.1)
Self-rated health (excellent, very good, good vs fair, poor) (%)	85.9	84.9
Depressive symptoms (≥3) (%)	9.0	9.4
Physically inactive (≤1 vigorous physical activity per week) (%)	71.2	71.8
Overweight (BMI=25–29 kg/m^2) (%)	40.5	40.1
Obese (BMI ≥30 kg/m^2) (%)	25.9	27.5
Moderate alcohol consumption (more than 0 and fewer than 2 drinks/day) (%)	32.5	32.4
Heavy drinking alcohol consumption (2+ drinks/day) (%)	6.5	6.6
Ever smoked (%)	56.0	56.0
Memory score ≥ 0.78 (20th centile) (%)	80.2	80.4
Neighbourhood physical disorder (mean, SD)	0.2 (0.2)	0.2 (0.2)
Neighbourhood cohesion (mean, SD)	0.8 (0.2)	0.8 (0.2)
Neighbourhood safety (% excellent, very good, good)	93.3	93.5
Neighbourhood social ties (mean, SD)	0.6 (0.3)	0.6 (0.3)

ADL, activities of daily living; BMI, body mass index; IADL, instrumental activities of daily living.

All neighbourhood measures have a range of 0–1, so the ORs are directly comparable across the variables, and coefficients represent the contrast of best possible to worst possible value (1 vs 0).

Outcomes

We evaluated two outcomes: onset of any ADL limitation and onset of any IADL limitation. At each interview, participants or proxy respondents reported whether they had difficulty in the past 30 days in performing five ADLs (getting across room, dressing, bathing, eating, and getting in and out of bed) and five IADLs (using a phone, managing money, taking medications, shopping for groceries, and preparing hot meals). Response options were 'yes,' 'no,' 'do not do', and 'refused'. 'Do not do' and 'refused' were coded as missing. Participants who answered in the affirmative for any ADL or any IADL were considered having an ADL or IADL limitation for that interview wave. We restricted the sample to those without the outcome of interest in the current or prior wave when the neighbourhood data was collected.

Memory function

Our measure of memory function was imputed memory scores, which have been described elsewhere.[12] Briefly, an immediate and delayed recall of a 10-item word list and the Telephone

Interview for Cognitive Status (TICS) were used to construct the memory scores. For participants too impaired to participate in the direct memory assessments, proxy informants completed the 16-item Jorm Informant Questionnaire for Cognitive Decline and a single-item memory impairment question. We created a dichotomous measure of memory impairment corresponding to approximately the 20th centile in our sample. Memory function in 2006 and 2008 were used for participants with neighbourhood data for 2006 and 2008, respectively. In sensitivity analyses, we modelled memory as a continuous variable but results were qualitatively similar, so we present models using dichotomised memory.

Covariates

Covariate data from 2004 and 2006 were used for participants with neighbourhood data for 2006 and 2008, respectively. Because several covariates could plausibly be conceptualised as confounders or as mediators, we built three successive models with adjustment for additional covariates in each model. In the first model, we adjusted for age (continuous), age squared (continuous), sex, race (black vs other), memory function (<20th centile or ≥20th centile) and wave of I/ADL assessment.

In model 2, we included additional demographic characteristics and socioeconomic status variables: southern birthplace (yes/no), years of education (linear spline model with discontinuities at completion of high school and college plus an indicator variable for General Educational Development (GED)), marital status (married, divorced/separated, widowed, never married), mother's and father's education (≤8 years, >8 years), height, height by sex interaction, log of household size-adjusted wealth, log of household size-adjusted income and employment status (currently working for pay, not working for pay).

In model 3, we added comorbidities and health behaviours: self-reported health (poor/fair vs good/very good/excellent), body mass index categories (<25, 25–29, 30+ kg/m^2), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), physical activity (vigorous physical activity >1 per week vs ≤ 1), alcohol consumption (no drinks, more than zero and fewer than 2 drinks/day, 2+ drinks/day), ever smoked (yes/no), depression (yes/no where yes was defined as reporting ≥3 depressive symptoms on a modified 8-item Centers for Epidemiologic Studies-Depression (CES-D) scale in the past two weeks). Neighbourhood context has been found to influence health behaviours such as physical activity,[10 13] smoking,[14] and alcohol consumption,[14] and health outcomes such as depressive symptoms[15] and self-reported health.[16] Since the third set of covariates includes several variables that were potentially affected by past neighbourhood context, we consider model 2 as the primary results and model 3 as supplementary analyses.

Statistical analyses

We fit discrete time survival models using pooled logistic regression to examine the associations between neighbourhood level factors and (1) ADL limitations and (2) IADL limitations. Estimates are ORs, which with rare outcomes approximate HRs in continuous time survival analysis. Individuals were censored at last interview, death or on developing the outcome of interest. To investigate whether memory modified the impact of neighbourhood characteristics on I/ADL limitations, we included interaction terms between memory and each neighbourhood characteristic.

To investigate these associations on an absolute scale, we calculated the marginal probabilities of developing I/ADL limitations by memory function and level of each neighbourhood factor by using the 'margins' command in Stata V.13. For physical disorder, social cohesion, and social ties, we compared participants rating neighbourhood characteristics at the 25th centile and at the 75th centile. For neighbourhood safety, we compared those who rated their neighbourhood as excellent, very good, or good versus those who rated their neighbourhood as fair or poor. The marginal probability by neighbourhood characteristics was calculated using coefficients estimated in the pooled logistic

Table 2 Association between neighbourhood level variables, IADL and ADL limitations

	Model 1			Model 2			Model 3		
	OR	95% CI		OR	95% CI		OR	95% CI	
Onset of IADLs (n=8726)									
Neighbourhood physical disorder	0.36	0.26	0.48	0.51	0.37	0.69	0.57	0.41	0.78
Neighbourhood social cohesion	0.36	0.27	0.47	0.46	0.34	0.62	0.54	0.40	0.73
Neighbourhood safety	0.50	0.39	0.64	0.59	0.46	0.76	0.67	0.51	0.87
Neighbourhood social ties	0.97	0.77	1.21	0.93	0.74	1.17	0.95	0.76	1.20
Composite measure	0.21	0.14	0.33	0.31	0.20	0.48	0.40	0.26	0.63
Onset of ADLs (n=8345)									
Neighbourhood physical disorder	0.43	0.32	0.58	0.59	0.43	0.81	0.70	0.50	0.96
Neighbourhood social cohesion	0.46	0.34	0.61	0.60	0.45	0.81	0.79	0.58	1.08
Neighbourhood safety	0.61	0.48	0.78	0.74	0.58	0.93	0.87	0.68	1.10
Neighbourhood social ties	0.98	0.77	1.23	1.01	0.80	1.28	1.04	0.82	1.32
Composite measure	0.32	0.21	0.49	0.49	0.32	0.76	0.71	0.45	1.10

All neighbourhood measures have a range of 0–1, so the ORs are directly comparable across the variables, and coefficients for physical disorder, social ties, social cohesion, and the composite measure represent the contrast between best possible and worst possible value (1 vs 0). For safety, the comparison is between those who rated their neighborhood as excellent, very good, or good versus those who rated their neighborhood as fair or poor.
Model 1 covariates: age, age squared, sex, race, memory, wave.
Model 2 covariates: model 1+southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), marital status (married, divorced/separated, widowed, never married), mother's and father's education (≤8 years, >8 years), height, height×sex interaction, log of household size-adjusted wealth, log of household size-adjusted income, and employment status (currently working for pay, not working for pay).
Model 3 covariates: model 2+self-reported health (poor, fair vs good, very good, excellent), body mass index (<25, 25–29, 30+), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), physical activity (active vs inactive), alcohol consumption (no drinks, more than zero and fewer than 2 drinks/day, 2+ drinks/day), ever smoked (yes/no), depression (yes/no where yes was defined as reporting ≥3 depressive symptoms on a modified 8-item Centers for Epidemiologic Studies-Depression (CES-D) scale in the past 2-weeks).
ADL, activities of daily living; IADL, instrumental and basic activities of daily living.

models and the actual population distribution of the other covariates. For marginal probabilities by memory status and neighbourhood characteristics, we estimated the probabilities stratified by memory status (≥ 20th centile and <20th centile), adjusting for covariates. All analyses were weighted using the HRS sampling weights in 2008.

RESULTS

Online supplementary figures S1 and S2 present flow charts of participants who met the exclusion/inclusion criteria for the study population (see online supplementary materials). During follow-up 1443 participants reported development of an IADL limitation, and 1377 reported development of an ADL limitation. The baseline characteristics of the participants are shown in table 1. Participants excluded from the analyses tended to be older, had fewer years of schooling, and were less likely to have a mother or father with greater than 8 years of education. They were also less likely to be married, less likely to be employed, and had lower memory scores than participants included in the analyses (see supplementary table S1).

Associations between neighbourhood level factors, memory and I/ADL limitations are presented in table 2. After adjustment for demographics and socioeconomic status (model 2), neighbourhood characteristics were associated with IADL incidence: (physical disorder OR=0.51 comparing the lowest to highest possible neighbourhood physical disorder (95% CI 0.37 to 0.69)); neighbourhood social cohesion (OR=0.46 comparing highest to lowest cohesion (95% CI 0.34 to 0.62)); neighbourhood safety (OR=0.59 comparing ratings of excellent/very good/good vs fair/poor (95% CI 0.46 to 0.76)); and the composite neighbourhood measure (OR=0.31 (95% CI 0.20 to 0.48)). These neighbourhood characteristics were also associated with incidence of ADL limitations (physical disorder OR=0.59 (95% CI 0.43 to 0.81)); social cohesion OR=0.60 (95% CI 0.45 to 0.81); safety OR=0.74 (95% CI 0.58 to 0.93); composite OR=0.49 (95% CI 0.32 to 0.76). Neighbourhood social ties were not related to IADLs (OR=0.93 (95% CI 0.74 to 1.17)) or ADLs (OR=1.01 (95% CI 0.80 to 1.28). In model 3, we adjusted for potential mediators such as self-reported comorbidities and health behaviours. The effects of physical disorder, social cohesion and safety on IADL limitations were attenuated. The effects of neighbourhood characteristics on ADL limitations were also attenuated and no longer statistically significant for social cohesion, safety and the composite measure.

Low neighbourhood physical disorder, high social cohesion, and high safety were protective for onset of IADLs among

Table 3 Association between neighbourhood-level variables and incident IADL limitations including interactions between neighbourhood variables and memory function (n=8726)

	Model 1				Model 2				Model 3			
	OR	95% CI		p Value	OR	95% CI		p Value	OR	95% CI		p Value
Neighbourhood physical disorder												
Normal memory	1.30	0.84	2.03	0.24	1.18	0.74	1.87	0.49	1.10	0.68	1.75	0.70
Neighbourhood physical disorder	1.37	0.91	2.05	0.14	0.90	0.59	1.38	0.63	0.91	0.59	1.41	0.67
Normal memory×disorder†	2.95	1.71	5.11	<0.001	0.41	0.23	0.73	<0.01	0.49	0.27	0.87	0.01
Neighbourhood social cohesion												
Normal memory	1.37	0.88	2.13	0.16	1.33	0.85	2.09	0.21	1.23	0.77	1.96	0.39
Neighbourhood social cohesion	0.74	0.50	1.10	0.13	0.88	0.59	1.33	0.56	0.94	0.61	1.44	0.77
Normal memory×cohesion†	0.32	0.19	0.54	<0.0001	0.36	0.21	0.62	<0.001	0.42	0.24	0.74	<0.01
Neighbourhood safety												
Normal memory	1.09	0.70	1.69	0.71	0.93	0.59	1.47	0.76	0.92	0.57	1.46	0.72
Neighbourhood safety	0.81	0.57	1.15	0.23	0.82	0.57	1.18	0.28	0.88	0.61	1.27	0.51
Normal memory×safety†	0.49	0.32	0.77	<0.01	0.63	0.40	1.00	0.05	0.67	0.42	1.08	0.10
Neighbourhood social ties												
Normal memory	0.81	0.59	1.12	0.20	0.83	0.60	1.15	0.27	0.86	0.62	1.19	0.36
Neighbourhood social ties	1.45	1.04	2.04	0.03	1.34	0.95	1.89	0.09	1.35	0.95	1.92	0.10
Normal memory×social ties†	0.56	0.36	0.86	0.01	0.59	0.38	0.92	0.02	0.61	0.39	0.96	0.03
Composite variable												
Normal memory	2.51	1.34	4.70	0.00	2.07	1.09	3.93	0.03	1.82	0.95	3.51	0.07
Composite measure	0.83	0.44	1.56	0.56	0.96	0.50	1.86	0.91	1.07	0.54	2.10	0.85
Normal memory×composite†	0.14	0.06	0.32	<0.0001	0.20	0.09	0.45	<0.001	0.25	0.11	0.57	<0.01

All neighbourhood measures have a range of 0–1, so the ORs are directly comparable across the variables, and coefficients for physical disorder, social ties, social cohesion, and the composite measure represent the contrast between best possible and worst possible value (1 vs 0). For safety, the comparison is between those who rated their neighborhood as excellent, very good, or good versus those who rated their neighborhood as fair or poor.
The coefficient for normal memory represents the comparison of participants with normal memory (≥20th centile) to participants with impaired memory (<20th centile) on incidence of IADL limitations; because of the interaction term included in the model, this estimate applies to participants with the worst possible neighbourhood characteristic score (0).
Model 1 covariates: age, age squared, sex, race, memory, wave.
Model 2 covariates: model 1+southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), marital status (married, divorced/separated, widowed, never married), mother's and father's education (=<8 years, >8 years), height, height×sex interaction, log of household size-adjusted wealth, log of household size-adjusted income, and employment status (currently working for pay, not working for pay).
Model 3 covariates: model 2+self-reported health (poor, fair vs good, very good, excellent), body mass index (<25, 25–29, 30+), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), physical activity (active vs inactive), alcohol consumption (no drinks, more than zero and fewer than 2 drinks/day, 2+ drinks/day), ever smoked (yes/no), depression (yes/no where yes was defined as reporting ≥3 depressive symptoms on a modified 8-item Centers for Epidemiologic Studies-Depression (CES-D) scale in the past two weeks).
†The interaction coefficient for memory by neighbourhood characteristic represents the estimated differential effect of the neighbourhood characteristic on incidence of IADL limitations among those with normal memory (≥20th centile) compared to those with impaired memory (<20th centile). An interaction coefficient <1 indicates the effect of the neighbourhood characteristic is more strongly and inversely associated with IADL limitations among those with normal memory than those with impaired memory.
IADL, instrumental activities of daily living.

participants with normal memory but the effects were attenuated and not statistically significant among participants with memory impairment (table 3). For example, high social cohesion was non-significantly associated with an OR of 0.88 for developing an IADL limitation among those with memory impairment (95% CI 0.59 to 1.33). Among those with normal memory function, high social cohesion was associated with an OR of 0.32 (0.88×0.36) for developing an IADL limitation (p value for interaction <0.001) (table 3). p Values for interaction between memory and each of the other neighbourhood characteristics were as follows: physical disorder p value: <0.01; neighbourhood safety p value: 0.05; social ties p value: 0.02; composite p value: <0.001). In contrast, there was no evidence of interactions on the relative scale between any of the neighbourhood factors and memory function (p ≥0.1 for all interactions) for onset of ADLs (table 4). Stratified results by memory function and neighbourhood characteristics are presented in online supplementary table S2.

Absolute probability estimates revealed a similar pattern as estimates on the relative scale. Low neighbourhood physical disorder and social cohesion (75th vs 25th centile) were associated with a 1 percentage point difference in 2-year incidence rate in IADL and ADL limitations. Comparing those rating their neighbourhood as safe (excellent/very good/good) versus unsafe (fair/poor), there was a 2–3 percentage point difference in 2-year incidence rate of IADL and ADL limitations (figure 1).

There was also evidence of differential impact of the neighbourhood characteristics by memory status on the absolute scale (see online supplementary table S3). Low physical disorder, high social cohesion and high safety were associated with a 1–3 percentage point lower incidence of IADL limitations among respondents with normal memory function. However, these neighbourhood characteristics were not related to IADLs among those with memory impairment. For ADLs, neighbourhood characteristics had similar effects for people with normal and impaired memory. Based on the observed 2-year cumulative incidence of ADL limitations in our cohort, the median time of onset of ADL limitations is 9.5 years for those with memory impairment living in low physical disorder neighbourhoods compared to 8.4 years for those with memory impairment living in high physical disorder neighbourhoods (see online supplementary materials for additional details on the calculations).

DISCUSSION

In models accounting for demographics and SES, low physical disorder, high neighbourhood social cohesion, and high

Table 4 Association between neighbourhood-level variables and incident ADL limitations including interactions between neighbourhood variables and memory function (n=8345)

	Model 1				Model 2				Model 3			
	OR	95% CI		p Value	OR	95% CI		p Value	OR	95% CI		p Value
Neighbourhood physical disorder												
Normal memory	0.70	0.45	1.12	0.14	0.64	0.40	1.03	0.06	0.57	0.35	0.93	0.03
Neighbourhood physical disorder	0.53	0.34	0.81	<0.01	0.66	0.43	1.02	0.06	0.66	0.42	1.05	0.08
Normal memory×disorder†	0.74	0.42	1.31	0.30	0.85	0.48	1.52	0.59	1.07	0.58	1.98	0.82
Neighbourhood social cohesion												
Normal memory	0.57	0.37	0.89	0.01	0.51	0.32	0.80	<0.01	0.44	0.27	0.72	0.001
Neighbourhood social cohesion	0.47	0.32	0.69	<0.001	0.55	0.37	0.82	<0.01	0.61	0.40	0.95	0.03
Normal memory×cohesion†	0.96	0.56	1.65	0.88	1.16	0.67	2.00	0.60	1.49	0.83	2.67	0.19
Neighbourhood safety												
Normal memory	0.76	0.49	1.18	0.22	0.67	0.43	1.05	0.08	0.63	0.40	0.99	0.04
Safety	0.77	0.56	1.07	0.12	0.84	0.60	1.16	0.29	0.90	0.64	1.26	0.53
Normal memory×safety†	0.70	0.45	1.09	0.11	0.83	0.53	1.29	0.40	0.95	0.60	1.50	0.82
Neighbourhood social ties												
Normal memory	0.69	0.49	0.95	0.02	0.70	0.50	0.98	0.04	0.72	0.51	1.01	0.06
Social ties	1.27	0.90	1.79	0.17	1.30	0.92	1.85	0.14	1.29	0.90	1.85	0.17
Normal memory×social ties†	0.69	0.44	1.08	0.10	0.69	0.44	1.10	0.12	0.74	0.46	1.18	0.20
Composite variable												
Normal memory	0.88	0.47	1.65	0.69	0.75	0.40	1.41	0.37	0.61	0.31	1.17	0.14
Composite measure	0.48	0.26	0.87	0.02	0.63	0.34	1.16	0.14	0.71	0.38	1.35	0.30
Normal memory×composite†	0.55	0.25	1.21	0.13	0.70	0.31	1.55	0.38	0.99	0.43	2.27	0.98

All neighbourhood measures have a range of 0–1, so the ORs are directly comparable across the variables, and coefficients for physical disorder, social ties, social cohesion, and the composite measure represent the contrast between best possible and worst possible value (1 vs 0). For safety, the comparison is between those who rated their neighborhood as excellent, very good, or good versus those who rated their neighborhood as fair or poor.
The coefficient for normal memory represents the comparison of participants with normal memory (≥20th centile) to participants with impaired memory (<20th centile) on incidence of ADL limitations; because of the interaction term included in the model, this estimate applies to participants with the worst possible neighbourhood characteristic score (0).
Model 1 covariates: age, age squared, sex, race, memory, wave.
Model 2 covariates: model 1+southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), marital status (married, divorced/separated, widowed, never married), mother's and father's education (≤8 years, >8 years), height, height×sex interaction, log of household size-adjusted wealth, log of household size-adjusted income, and employment status (currently working for pay, not working for pay).
Model 3 covariates: model 2+self-reported health (poor, fair vs good, very good, excellent), body mass index (<25, 25–29, 30+), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), physical activity (active vs inactive), alcohol consumption (no drinks, more than zero and fewer than 2 drinks/day, 2+ drinks/day), ever smoked (yes/no), depression (yes/no where yes was defined as reporting ≥3 depressive symptoms on a modified 8-item Centers for Epidemiologic Studies-Depression (CES-D) scale in the past two weeks).
†The interaction coefficient for memory by neighbourhood characteristic represents the estimated differential effect of the neighbourhood characteristic on incidence of ADL limitations among those with normal memory (≥20th centile) compared to those with impaired memory (<20th centile). An interaction coefficient <1 indicates the effect of the neighbourhood characteristic is more strongly and inversely associated with ADL limitations among those with normal memory than those with impaired memory.
ADL, activities of daily living; IADL, instrumental activities of daily living.

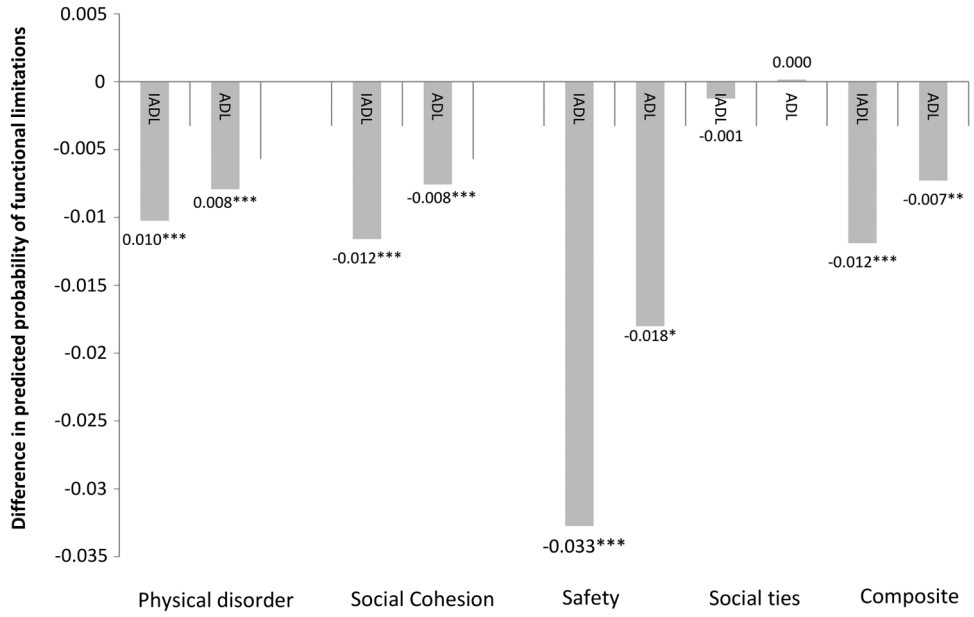

Figure 1 Absolute difference in 2-year incidence rate in IADL and ADL limitations by level of neighbourhood factors, comparing participants rating neighbourhood characteristics at the 75th to 25th centile for physical disorder, social cohesion, social ties and the composite measure. For neighbourhood safety, we compared those who rated their neighbourhood as excellent, very good, or good versus those who rated their neighbourhood as fair and poor. p Values for the test that the differences are equal to zero. *p<0.05, **p<0.01, ***p<0.001. ADL, activities of daily living; IADL, instrumental and basic activities of daily living.

neighbourhood safety were associated with reduced incidence of IADL and ADL limitations. Neighbourhood social ties were not associated with IADL or ADL limitations. The estimated benefits of neighbourhood characteristics for ADL limitations were similar for people with and without memory impairment. The relative and absolute effects of neighbourhood physical disorder, social cohesion, and safety on IADL limitations were attenuated among participants with memory impairment.

Previous reviews on the influence of the neighbourhood environment on health and mobility in older adults found that most studies were cross-sectional and used objective neighbourhood measures.[5 6] In our longitudinal study, perceived neighbourhood characteristics were associated with onset of functional limitations.

We found that the impact of neighbourhood characteristics on IADLs were diminished among those with memory impairment compared to those with normal memory function. This is consistent with previous research, showing that among people with memory impairment, it is easier to delay onset of ADL than IADL disability.[17 18] We hypothesise this is due to the close link between cognitive function and IADLs.

This paper has several strengths. We used a large, national study of older adults and used a prospective cohort design. We controlled for a comprehensive list of demographics, individual characteristics and cognitive function to reduce confounding.

Limitations include generalisability since we restricted the sample to those without prior I/ADL limitations. Included participants tended to be younger and have higher socioeconomic status than those excluded. Limitations also include the potential for residual unmeasured confounding because this is an observational study. Additionally, we only have data on the participant's neighbourhood of residence at the time of data collection. Neighbourhood environment was assessed through self-report, which may be influenced by cognitive function. However, we controlled for memory function in all models.

The public health importance of these effect estimates depends on the extent to which it is possible to change these neighbourhood characteristics. To facilitate direct comparison of effect estimates, we transformed the physical disorder and social cohesion measures to match the range of the other neighbourhood variables (ranging from 0 to 1). However, very few individuals reported the most extreme values of these variables; for example, only 15% of respondents reported the lowest possible level of disorder and less than 1% reported the highest possible value. Thus, the effect estimates for a one unit change (from 0 to 1) may present an overly optimistic estimate of the potential magnitude of effect.

This study found individuals who reported their neighbourhoods as having low disorder, higher levels of safety, and social cohesion had lower risk of incident I/ADL limitations. Neighbourhoods appeared relevant for onset of ADL limitations even for individuals with memory impairment. Efforts to improve neighbourhood safety conditions, reduce disorder and promote social cohesion may be beneficial for preventing or delaying onset of ADL limitations regardless of memory status and may be beneficial in reducing IADL limitations among those without memory impairment.

What is already known on this subject

Studies examining the influence of neighbourhood level factors on disability have primarily used objective measures of neighbourhood characteristics, been cross-sectional in design, and not been nationally representative. While some studies have observed that neighbourhood characteristics were related to functional limitations, research has not evaluated whether these neighbourhood characteristics are important for individuals with memory impairment.

What this study adds

We used a national, longitudinal study of older Americans to examine the impact of self-reported neighbourhood physical disorder, safety, social cohesion and social ties on incident functional limitations. We found that low neighbourhood physical disorder, high safety and high social cohesion were associated reduced onset of ADL and IADL limitations. These neighbourhood characteristics were important for activities of daily living (ADL) limitations regardless of memory function, but were principally protective for participants without memory impairment for instrumental and basic ADL limitations.

Correction notice This article has been corrected since it published Online First. Acronym expansions in tables 2 and 3 have been corrected to match text.

Contributors TTN and MMG were involved in the study design, data interpretation, and writing. TTN conducted the statistical analysis and prepared the first version of the manuscript. PMR was involved in the statistical analysis and data interpretation. All authors read and approved the final draft.

Funding This work was supported by the Telemedicine and Advanced Technology Research Center (TATRC) at the U.S. Army Medical Research and Materiel Command (USAMRMC) through award W81XWH- 12-1-0143.

Competing interests None declared.

Ethics approval University of California, San Francisco Institutional Review Board.

Provenance and peer review Not commissioned; externally peer reviewed.

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Dementia and dependence: Do modifiable risk factors delay disability?

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Neurology 2014;82;1543-1550 Published Online before print March 28, 2014
DOI 10.1212/WNL.0000000000000357

Dementia and dependence

Do modifiable risk factors delay disability?

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ABSTRACT

Objective: To identify modifying factors that preserve functional independence among individuals at high dementia risk.

Methods: Health and Retirement Study participants aged 65 years or older without baseline activities of daily living (ADL) limitations (n = 4,922) were interviewed biennially for up to 12 years. Dementia probability, estimated from direct and proxy cognitive assessments, was categorized as low (i.e., normal cognitive function), mild, moderate, or high risk (i.e., very impaired) and used to predict incident ADL limitations (censoring after limitation onset). We assessed multiplicative and additive interactions of dementia category with modifiers (previously self-reported physical activity, smoking, alcohol consumption, depression, and income) in predicting incident limitations.

Results: Smoking, not drinking, and income predicted incident ADL limitations and had larger absolute effects on ADL onset among individuals with high dementia probability than among cognitively normal individuals. Smoking increased the 2-year risk of ADL limitations onset from 9.9% to 14.9% among the lowest dementia probability category and from 32.6% to 42.7% among the highest dementia probability category. Not drinking increased the 2-year risk of ADL limitations onset by 2.1 percentage points among the lowest dementia probability category and 13.2 percentage points among the highest dementia probability category. Low income increased the 2-year risk of ADL limitations onset by 0.4% among the lowest dementia probability category and 12.9% among the highest dementia probability category.

Conclusions: Smoking, not drinking, and low income predict incident dependence even in the context of cognitive impairment. Regardless of cognitive status, reducing these risk factors may improve functional outcomes and delay institutionalization. ***Neurology*® 2014;82:1543–1550**

GLOSSARY

ADL = activities of daily living; **CI** = confidence interval; ***DSM-III-R*** = *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edition, revised; ***DSM-IV*** = *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition; **HRS** = Health and Retirement Study; **IPW** = inverse probability weighting; **OR** = odds ratio.

Cognitive impairment causes losses in independence in daily activities,[1] which hasten institutionalization.[2] Little prior research has examined whether factors that delay disability in cognitively normal adults have similar benefits among the cognitively impaired.

We hypothesized that onset of impairments in functional independence among individuals with cognitive impairment may be substantially accelerated by modifiable individual risk factors. This hypothesis is rooted in understanding of disability as emerging when physical impairments in body functioning or structure occur and it is not possible to adopt environmental, behavioral, and instrumental accommodations to overcome these impairments (see figure 1).[3,4] Individual-level modifiers, such as physical inactivity, alcohol consumption, smoking, depression, and low household income, may influence both the development of physical impairments and patients' ability to use accommodations or coping strategies. Cognitive impairment may also affect basic activities of daily living (ADL) independence because it reduces the patient's ability to adopt accommodations

Supplemental data at Neurology.org

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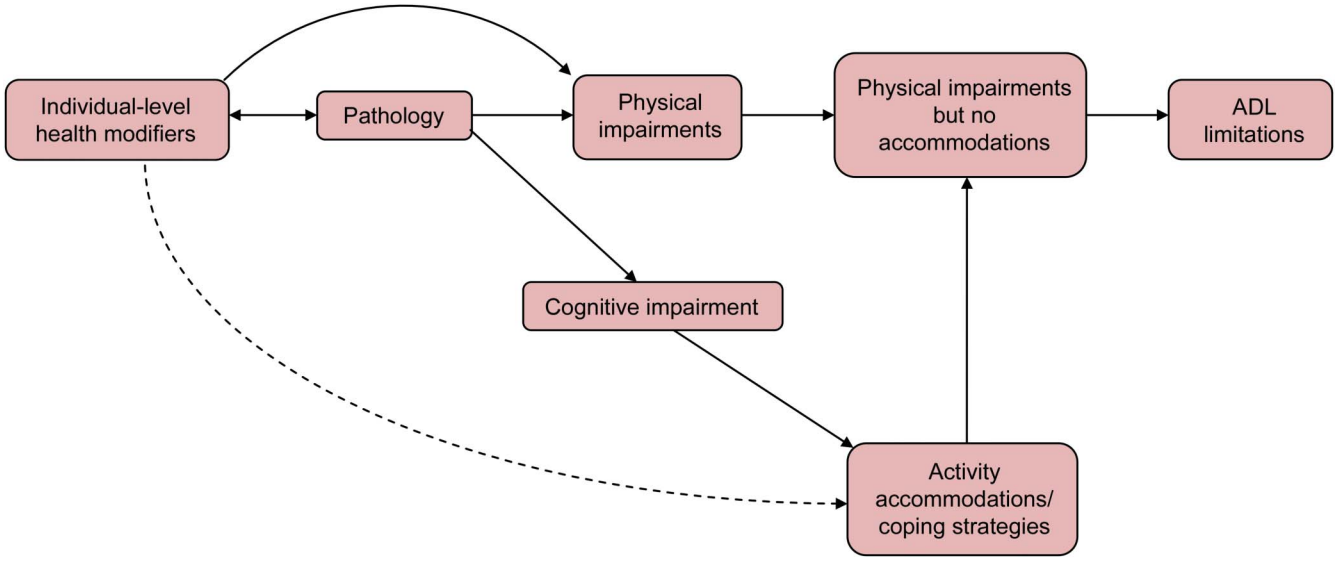
Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure 1 Hypothesized influence of individual-level health modifiers and cognitive impairment on the disablement process



An adaptation of the disablement process model by Verbrugge and Jette,[4] this figure illustrates how the co-occurrence of illness pathology and cognitive impairment leads to functional limitations and disability by impairing the patient's ability to adopt accommodations and coping strategies. ADL = activities of daily living.

or coping strategies. The combination of individual modifying risk factors and cognitive status will determine whether the patient is able to successfully use activity accommodations to interrupt the translation of physical impairments into ADL limitations. Assessing whether these individual risk factors modify the translation of cognitive impairments into disability has clinical importance because many of these factors may be insufficiently managed among patients with dementia.[5]

METHODS The Health and Retirement Study (HRS) is a nationally representative longitudinal survey of Americans aged 50 years or older and their spouses.[6,7] Participants were enrolled in 1992, 1993, and 1998 and were interviewed biannually through 2010.

Standard protocol approvals, registrations, and patient consents. The HRS was approved by the University of Michigan Health Sciences Human Subjects Committee. These analyses were determined exempt by the Harvard School of Public Health Office of Human Research Administration.

Outcome assessment. The outcome for this study was self-reported or proxy-reported (approximately 4% per wave) difficulty in 5 ADL (getting across a room, dressing, bathing, eating, and getting in and out of bed) in the past 30 days. Possible response options were yes, no, or do not do, which was treated as missing in this analysis. We looked at each activity individually and also used an indicator for any activity limitation, capturing limitations in any of the 5 ADL (based on the RAND HRS coding[8]).

Exposure status. Our primary exposure was imputed dementia probability score, a measure of cognitive impairment. Methods for calculating this score have been described in detail elsewhere.[9] Briefly, for participants too impaired to participate in interviews (approximately 2% per wave), proxies completed the Jorm Informant Questionnaire for Cognitive Decline and a single-item memory impairment question. Respondents able to participate in interviews completed immediate and delayed recall of 10-word lists and a modified Telephone Interview for Cognitive Status. In a subsample of participants, these items were combined and calibrated against dementia diagnosis according to *DSM-III-R* and *DSM-IV* criteria (C statistic = 94.3%). The dementia probability score corresponds to the estimated probability that the individual had dementia at interview per this calibration. For our analyses, the dementia probability score was divided into 4 categories (0 to ≤0.25, 0.25 to ≤0.50, 0.50 to ≤0.75, and 0.75 to ≤1), which represent low, mild, moderate, and high probability of developing dementia. The category of 0 to ≤0.25 (normal cognitive function) was used as the reference group for all analyses. In our longitudinal analyses, dementia probability score was assessed in the wave before ADL outcome assessment.

In secondary analyses, we used an imputed memory score as our measure of cognitive impairment and observed similar results (see appendix e-1 on the *Neurology*® Web site at Neurology.org).

Assessment of individual-level modifiers. We were interested in determining whether 5 self-reported or proxy-reported (approximately 2% per wave) individual-level factors (physical activity, drinking alcohol, smoking, depression, and income) predict similar reductions in the risk of incident ADL limitations regardless of level of cognitive impairment. Furthermore, we wanted to know whether these factors ameliorate or exacerbate the effects of cognitive impairment on incident ADL limitations, i.e., whether they interact with the cognitive impairment measures in predicting incident ADL limitations. Because of changes in the assessment of physical activity levels over time, physical activity was dichotomized as active vs inactive with active defined as vigorous activity ≥3 times per week in 1998 to 2002 and >1 time per week from 2004 onward (the closest available category to the previously used ≥3 times per week

cutpoint). Alcohol consumption was dichotomized into moderate drinking (more than 0 but fewer than 2 drinks per day) vs not drinking. Because of the low number of participants consuming 2 or more drinks per day, we excluded these individuals from our analyses of alcohol consumption, dementia category, and incident ADL limitations. Sensitivity analyses contrasting moderate drinkers with nonmoderate drinkers (nondrinkers or heavy drinkers) showed similar results to those presented here. Current smoking status was dichotomized (yes/no). An indicator variable for depression was constructed based on reporting ≥3 depressive symptoms on a modified 8-item Centers for Epidemiologic Studies–Depression Scale in the past 2 weeks. This threshold has been shown to have high sensitivity (71%) and specificity (79%) for depression per the Composite International Diagnostic Interview–Short Form.[10] We constructed an indicator variable for low income using a cutpoint of $12,031 (based on the 25th percentile of the household size–adjusted income at baseline). Modifier information was assessed in the wave before outcome assessment.

Covariates. We adjusted for the following potential time-constant confounders: age (centered, continuous), age squared, sex, race (black vs other), southern birthplace, education (modeled as linear terms for years of education with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), mother's and father's education (≤8 years vs >8 years), and height (sex-specific baseline quartiles). In addition, we adjusted for the following time-varying confounders: marital status (divorced/separated, widowed, never married, married), log of household size–adjusted wealth (continuous), body mass index (continuous), self-reported comorbidities (yes/no indicators for high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), interview wave, and our modifiers. Time-constant confounders were assessed at study baseline (1998) and time-updated confounders were assessed at the wave before the exposure. Those missing information on any covariates at baseline were excluded from our analyses. If the covariate was missing during follow-up, the last reported value was carried forward.

Statistical analysis. Pooled logistic regression models were used to calculate odds ratios (ORs), which with rare outcomes approximates a hazard ratio as in continuous time survival analyses. The relationship of the dementia probability categories with risk of ADL limitations was approximately linear, so the categories were treated as a linear variable. Participants were censored from analysis after last interview, onset of activity limitations, death, or at first wave of missing information on dementia probability. We used inverse probability weighting (IPW) to adjust for potential time-varying confounding. IPW required one wave of "run-in" (see below), so our first "exposure" wave was in 2000 and our first "outcome" wave was in 2002. Those who reported ADL limitations in 1998 or 2000 were excluded from our analyses.

To assess whether any of our modifiers ameliorated or exacerbated the effects of dementia score on ADL limitations, 2 different approaches were used. First, we included an interaction term between dementia score category and each modifier (in separate models for each modifier) to test whether each modifier had different relative effects on ADL limitations depending on the participant's dementia score. Next, to compare the absolute effects of each modifier in participants with highest or lowest dementia score, we calculated the marginal probability of developing an activity limitation according to modifier status and dementia category. If effects of any risk factor are precisely multiplicative, the absolute benefit for individuals with cognitive impairment will be larger. These probabilities were calculated using the coefficients estimated in the logistic models with interaction terms and the actual population distribution of other covariates. The marginal probabilities were then compared based on the predicted population incidence rate of ADL limitations if everyone in the population had: (1) low dementia probability and the "beneficial" value of the modifier; (2) low dementia probability and the "adverse" value of the modifier; (3) high dementia probability and the "beneficial" value of the modifier; or (4) high dementia probability and the "adverse" value of the modifier. All analyses were performed using PROC SURVEYLOGISTIC in SAS 9.2 (SAS Institute, Cary, NC) and Stata 12 (StataCorp, College Station, TX) with weights as described below.

We used IPW to avoid introducing bias by adjusting for variables potentially affected by prior exposure but which affect future exposure. We constructed 4 weights: "treatment" (category of dementia score), modifier status (separate weights were calculated for each modifier), survival, and participation in HRS. These weights were multiplied to create a weight for each observation reflecting the inverse probability that the individual was alive and participated in the outcome wave, and had the dementia and modifier values he or she actually had, given past dementia, modifier, and covariate history. We additionally included the HRS sampling weight from 1998. Weights were stabilized[11] and truncated at the 98th percentile to minimize the influence of outliers.

We had 4,922 individuals eligible for our analysis of the association between dementia score and any ADL limitation (see figure e-1 for exclusions). For analyses of onset of specific ADL limitations, the exact number of individuals eligible differs slightly for each ADL because of differences in the baseline prevalence of each ADL limitation.

RESULTS Most respondents (94.2%) had low dementia probability at baseline (table 1) and throughout follow-up (table 2).

Higher dementia probability score category was associated with increased risk of incident ADL limitations, with a per-category OR of 1.65 (95% confidence interval [CI]: 1.49, 1.83) (results not shown). This implies that individuals with the highest dementia category (>75% probability of dementia) had 4.48 times the odds of onset of ADL limitations as individuals in the lowest dementia category (≤25% probability of dementia).

Table 3 shows the association between dementia probability category and risk of incident ADL limitations, the association between each modifier and incident ADL limitations, and the interaction coefficient between dementia probability and each modifier. In these models, an interaction coefficient of 1 indicates that the modifier has the same relative effect on ADL limitations regardless of dementia probability; if the interaction coefficient is less than 1, it indicates that the modifier effect is lower (less harmful) among those with higher dementia probability.

For the outcome of any ADL limitation, among the physically active, each unit increase in dementia

Table 1 Baseline characteristics of participants included in the analysis of dementia probability category and any incident activities of daily living limitations by dementia probability category at baseline

	Dementia probability category			
	0–0.25 (n = 4,636)	0.25–0.50 (n = 146)	0.50–0.75 (n = 65)	0.75–1 (n = 75)
Age, y, mean (SD)	72.4 (5.6)	80.0 (6.8)	81.2 (6.0)	80.6 (6.7)
Sex, % male	43.7	41.8	29.2	22.7
Race, % black	9.1	19.9	15.4	24.0
Southern birthplace, %	12.7	20.6	15.4	22.6
Years of education, mean (SD)	12.6 (2.8)	10.8 (3.5)	9.9 (3.4)	9.9 (3.9)
Mother had ≥8 y of education, %	53.0	45.9	36.9	33.3
Father had ≥8 y of education, %	45.5	41.1	30.8	33.3
Height, m, mean (SD)	1.7 (0.1)	1.7 (0.1)	1.6 (0.1)	1.6 (0.1)
Marital status, %				
Married	65.5	48.0	40.0	41.3
Divorced/separated	6.3	5.5	9.2	5.3
Widowed	24.7	43.2	49.2	52.0
Never married	3.5	3.4	1.5	1.3
Not physically active, %	51.3	63.7	69.2	84.0
Nondrinker, %	74.8	87.1	92.2	94.7
Current smoking, %	8.9	10.3	1.5	4.0
Current depression, %	9.3	19.2	13.9	17.3
Low household size–adjusted income, %	18.4	39.0	50.8	50.7
Body mass index, kg/m^2, mean (SD)	26.1 (4.2)	25.4 (4.0)	24.2 (4.4)	24.4 (4.0)
No. of comorbidities, mean (SD)	1.5 (1.2)	1.6 (1.1)	1.6 (1.3)	1.4 (1.2)

category was associated with an OR of 1.83 (95% CI: 1.36, 2.46). Low physical activity was associated with an increase in incident ADL limitations among those with the lowest dementia probability OR = 1.51 (95% CI: 1.25, 1.81). The interaction between physical activity and dementia probability was close to 1 and not significant (OR = 0.86; 95% CI: 0.63, 1.18), indicating that the estimated relative harm of low physical activity was similar regardless of dementia category. Depression was also associated with an increased risk of ADL limitations and the interaction between depression and dementia probability suggested that depression may be less harmful, in relative terms, among the cognitively impaired (OR = 0.72; 95% CI: 0.56, 0.92). Not drinking, smoking, and low income were not associated with an increased risk

Table 2 Distribution of dementia probability score and number of any incident ADL limitations by year

	Year					
	2002	2004	2006	2008	2010	Any incident ADL limitation
Dementia probability category, n (%)						
0–0.25	4,636 (94.2)	3,724 (93.7)	3,024 (93.1)	2,379 (92.3)	1,819 (91.8)	1,493 (80.2)
0.25–0.50	146 (3.0)	119 (3.0)	106 (3.3)	105 (4.1)	87 (4.4)	131 (7.0)
0.50–0.75	65 (1.3)	68 (1.7)	54 (1.7)	49 (1.9)	41 (2.1)	92 (4.9)
0.75–1	75 (1.5)	63 (1.6)	66 (2.0)	45 (1.8)	34 (1.7)	145 (7.8)
Any incident ADL limitation, n	536	390	378	298	259	1,861
Died this wave, n	0	255	239	216	205	915
Did not respond, n	0	157	95	78	94	424

Abbreviation: ADL = activities of daily living.
Percentages may not add to 100% because of rounding.

Table 3 Association between dementia category and incident ADL limitations including interactions between dementia category and individual health factors

	Any ADL limitation	Walking	Dressing	Eating	Getting in/out of bed	Bathing
Physical activity						
Dementia category	1.83 (1.36, 2.46)	1.57 (1.16, 2.14)	2.25 (1.70, 2.98)	2.62 (1.93, 3.56)	1.78 (1.32, 2.39)	2.71 (2.08, 3.54)
Dementia × no physical activity	0.86 (0.63, 1.18)	0.96 (0.70, 1.32)	0.71 (0.53, 0.95)	0.68 (0.49, 0.93)	0.90 (0.65, 1.22)	0.64 (0.48, 0.85)
No physical activity	1.51 (1.25, 1.81)	1.51 (1.15, 2.00)	1.69 (1.35, 2.13)	1.98 (1.39, 2.82)	1.78 (1.32, 2.40)	2.22 (1.69, 2.92)
Drinking						
Dementia category	1.27 (0.88, 1.83)	1.58 (1.10, 2.26)	1.41 (0.95, 2.09)	2.01 (1.43, 2.81)	1.67 (1.17, 2.39)	1.90 (1.39, 2.59)
Dementia × not drinking	1.28 (0.87, 1.87)	0.95 (0.65, 1.39)	1.21 (0.81, 1.81)	0.87 (0.61, 1.23)	0.96 (0.67, 1.38)	0.91 (0.66, 1.26)
Not drinking	1.22 (0.96, 1.56)	1.43 (1.04, 1.97)	1.23 (0.92, 1.65)	1.15 (0.77, 1.73)	1.47 (1.00, 2.17)	1.34 (0.97, 1.85)
Smoking						
Dementia category	1.68 (1.51, 1.86)	1.59 (1.43, 1.77)	1.72 (1.53, 1.92)	1.80 (1.59, 2.03)	1.64 (1.45, 1.85)	1.90 (1.72, 2.11)
Dementia category × smoking	0.99 (0.39, 2.54)	0.87 (0.38, 1.99)	0.61 (0.30, 1.25)	0.34 (0.16, 0.72)	0.68 (0.37, 1.27)	0.50 (0.21, 1.22)
Smoking	1.63 (0.94, 2.82)	1.37 (0.69, 2.71)	1.27 (0.66, 2.41)	2.49 (1.21, 5.13)	2.03 (0.97, 4.28)	2.16 (1.19, 3.92)
Depression						
Dementia category	1.71 (1.51, 1.93)	1.62 (1.43, 1.83)	1.78 (1.57, 2.01)	1.99 (1.74, 2.28)	1.67 (1.47, 1.89)	1.94 (1.72, 2.19)
Dementia × depression	0.72 (0.56, 0.92)	0.89 (0.65, 1.22)	0.78 (0.62, 0.98)	0.74 (0.55, 1.00)	1.05 (0.77, 1.42)	0.89 (0.67, 1.19)
Depression	1.59 (1.27, 2.01)	1.69 (1.31, 2.17)	1.54 (1.21, 1.95)	2.65 (1.91, 3.70)	1.53 (1.14, 2.06)	1.47 (1.14, 1.89)
Income						
Dementia category	1.58 (1.36, 1.82)	1.76 (1.52, 2.04)	1.89 (1.63, 2.19)	2.11 (1.75, 2.55)	1.96 (1.65, 2.32)	2.11 (1.82, 2.45)
Dementia × low income	1.24 (0.91, 1.70)	0.75 (0.55, 1.02)	0.91 (0.71, 1.17)	0.93 (0.71, 1.23)	1.02 (0.77, 1.34)	1.15 (0.87, 1.54)
Low income	0.95 (0.74, 1.23)	1.30 (0.96, 1.75)	0.93 (0.72, 1.21)	1.32 (0.89, 1.96)	1.05 (0.74, 1.49)	0.92 (0.68, 1.23)

Abbreviation: ADL = activities of daily living.
Data are odds ratio (95% confidence interval). We adjusted for the following potential time-constant confounders: age, age squared, sex, race, southern birthplace, education, mother's and father's educations, and height. In addition, we adjusted for the following time-varying confounders using an inverse probability weighting approach: marital status, log of household size–adjusted wealth, body mass index, self-reported comorbidities, interview wave, and our modifiers.

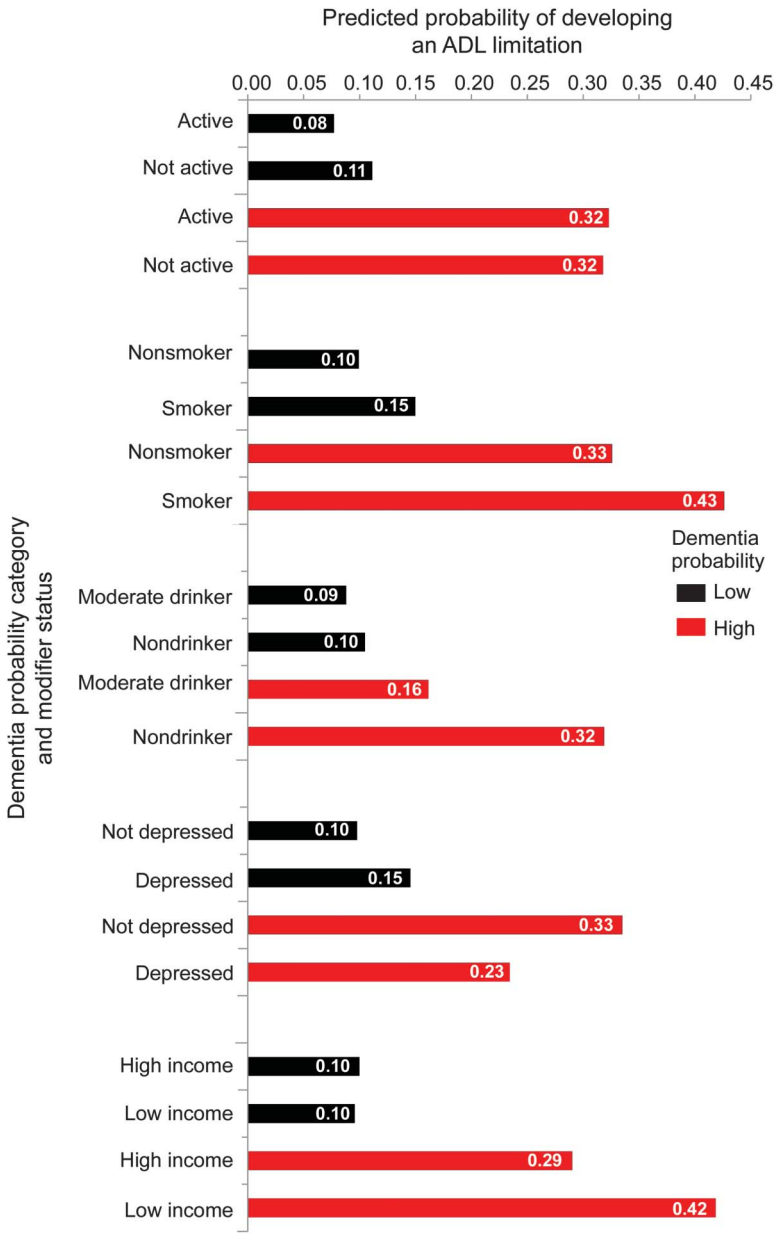
of ADL limitations and the interaction between these modifiers and dementia was also close to the null, suggesting that the relative harm of not drinking, smoking, or low income was similar regardless of dementia probability.

We also calculated the marginal probability of developing any incident ADL limitations for each combination of modifier status and lowest or highest dementia category (figure 2). For example, individuals in the lowest dementia category who are smokers have a 15.0% probability of developing any incident ADL limitation within 2 years. If a similar person is a nonsmoker, the 2-year probability of developing an ADL limitation is only 9.9%, thus not smoking predicts a 5.1 percentage point decrease in the probability of incident ADL limitations among those with low dementia probability. Smokers with the highest dementia scores have a 42.6% chance of developing an ADL limitation within 2 years, but physically active individuals with high dementia probability have only a 32.6% chance of developing any incident ADL limitation within 2 years. Not smoking predicts a 10.0 percentage point decrease in the probability of incident ADL limitations among individuals who are in the highest dementia probability category. Therefore, the absolute effect of not smoking is predicted to be larger among those with higher dementia probability. Not drinking and low income are also predicted to have larger adverse effects on the absolute probability of developing incident ADL limitations among those with high dementia probability than among those with low dementia probability.

DISCUSSION Results from this large prospective cohort study indicate that the relative impact of modifiable risk factors on incident ADL limitations was quite similar for all levels of cognitive functioning. Because disability is more prevalent among individuals with cognitive impairment, some modifiable risk factors had larger absolute benefits for individuals at high risk of dementia. This suggests that even among individuals with substantial cognitive impairment, managing conventional risk factors is very important.

Many of our individual-level modifiers are established predictors of functional decline among healthy elderly, but little evidence exists about whether these

Figure 2 **Marginal predicted probability of any ADL limitation per wave by modifier and dementia status**



Bar lengths represent actual numbers before rounding. Activities of daily living (ADL) limitations were assessed each wave (every 2 years). We adjusted regression models for the following potential confounders: age, age squared, sex, race, southern birthplace, education, mother's and father's educations, and height. In addition, we accounted for the following time-varying confounders using an inverse probability weighting approach: marital status, log of household size–adjusted wealth, body mass index, self-reported comorbidities, interview wave, and our modifiers.

advantages generalize to populations with cognitive impairment.[12] Smoking and depression have repeatedly been linked to disability measures.[13–18] Evidence on alcohol consumption and disability has been mixed.[15,19] Moderate alcohol consumption may have a protective effect for general physical functioning, but high consumption may be harmful.[20] While this study does not specifically assess the impact of initiating alcohol consumption, it suggests that efforts to reduce alcohol consumption may not improve ADL outcomes.

Research has typically focused on the impact of these modifiers on disability or functional limitations among cognitively normal adults,[13,15–17,19] although there is research on the effects of physical activity among those with cognitive impairment. A recent review found that physical activity was beneficial for physical functioning and ADL for mild, moderate, and severe dementia.[21] Some physical activity interventions have also been shown to improve physical functioning in older people with dementia.[22]

Our results on the continuing importance of modifiable risk factors among individuals with cognitive impairments have a great deal of clinical relevance. Conventional risk factors for ADL limitations, such as depression, are often undertreated among those with cognitive impairment.[5] Even traditional vascular risk factors, such as high blood pressure, dyslipidemia, diabetes mellitus, smoking, and atherosclerotic disease, may be untreated in those with cognitive impairment.[23] However, healthy risk factor profiles may help individuals with incipient dementia maintain functional independence, thereby avoiding institutionalization and decreasing caregiver burden.

We hypothesize that cognitive impairment may result in functional limitations through a multistep process. Cognitive function may be most relevant for maintaining independence among individuals with some level of physical impairments, who need to adopt behavioral accommodations or adaptive equipment to maintain independence. Because conventional risk factors delay physical impairments, they are very valuable for delaying dependence among individuals with cognitive impairment. For example, physical activity, smoking, alcohol use, and depression have all been linked to cardiovascular disease and other pathologies. Cognitive losses and conventional risk factors may create unfortunate cascades in which one reinforces the other, ultimately culminating in disability. For example, an individual with cognitive impairment may curtail independent leisure time walks or other physical activity because of safety concerns. Recognition of memory losses may lead to sadness and depression among older adults.

As with all observational research, we cannot rule out unmeasured confounding and therefore cannot infer that the observed effects are causal. Physical impairments may affect the risk factors we examined, thus confounding associations between, for example, physical activity and incident ADL limitations. This study only focused on incident ADL limitations and did not consider instrumental ADL, which may be more strongly correlated with cognition.[24] While the modifiable risk factors may provide ways of

ameliorating the harmful effect of dementia probability, dementia probability is still a strong risk factor for incident ADL limitations. We do not have information on lifetime behavior history and cannot determine whether the beneficial associations are only present among those who have always practiced healthy behaviors. In addition, our measure of depression may not capture differences in depression severity appropriately in individuals with cognitive impairment. Differences in depression severity may be one possible explanation for the unexpected finding that depression may be less harmful, in relative terms, among those with cognitive impairment. We do not know when exactly within the 2-year time period between assessments that the ADL limitation developed. However, we used information on cognitive status and health modifiers from the wave before ADL assessment to avoid reverse causation. Finally, we did not examine disability fluctuations in this study. An exploratory analysis of our data found that those in the highest dementia probability category had lower odds of transitioning out of ADL limitations than those in the lowest dementia probability category. Therefore, by not examining fluctuations in ADL disability, we believe that our results are conservative estimates of the beneficial effects of our health modifiers. Because those with the highest dementia probability are the least likely to transition out of the disability state, preventing the onset of ADL limitations is important.

Among the strengths of this study is that it included a nationally representative sample with a long prospective follow-up; the longitudinal data allowed construction of a statistical model reflecting the hypothesized temporal sequencing of these factors. Given the potential dynamic feedback between cognitive impairment and other risk factors, we used IPW, currently the best available statistical tool to handle time-varying confounders and selective attrition. By using imputed dementia categories, we were able to use information from proxy reports of cognitive status instead of excluding individuals with more severe cognitive impairments. We examined both relative and absolute effects; absolute effect estimates are most relevant for evaluating public health impact.[25]

Smoking, not drinking, and having low income may increase the risk of incident ADL limitations among those with cognitive impairments. This finding has critical importance for clinicians, patients, and family members of individuals with cognitive impairments or incipient dementia. By managing conventional risk factors, it may be possible to stave off dependencies, maximize quality of life, and minimize caregiver burden.

AUTHOR CONTRIBUTIONS

Pamela M. Rist: drafting/revising the manuscript for content, including medical writing for content, study concept or design, and analysis or interpretation of data. Benjamin D. Capistrant, Qiong Wu, and Jessica R. Marden: interpretation of data and revising the manuscript for content. M. Maria Glymour: obtaining funding, study concept or design; interpretation of data, revising the manuscript for content, and supervision.

STUDY FUNDING

This work is/was supported by the Telemedicine and Advanced Technology Research Center at the US Army Medical Research and Materiel Command through award W81XWH-12-1-0143. Dr. Capistrant was supported by the NIH (T32 HD007168 and R24 HD050924).

DISCLOSURE

P. Rist has received funding from a training grant from the National Institute of Aging, from the Rose Traveling Fellowship Program in Chronic Disease Epidemiology and Biostatistics from the Harvard School of Public Health, and from a travel fund from the Department of Epidemiology at the Harvard School of Public Health. B. Capistrant receives funding from 2 NIH grants (T32 HD007168 and R24 HD050924). Q. Wu and J. Marden report no disclosures relevant to the manuscript. M. Glymour has received funding from the NIH, the Robert Wood Johnson Health & Society Program, the American Heart Association, and the Telemedicine and Advanced Technology Research Center at the US Army Medical Research and Materiel Command through award W81XWH-12-1-0143. Go to Neurology.org for full disclosures.

Received June 29, 2013. Accepted in final form January 28, 2014.

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